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14. ABSTRACT

The purpose of the present study is to better characterize and differentiate the effects of combat stress and explosive blast on the brain. To achieve this goal we have been collecting extensive data on brain structure and function using sophisticated magnetic resonance imaging (MRI) sequences and high density quantitative electroencephalography (EEG) recordings. We have also assessed the emotional health of troops via clinical interview and self-report measures. We have collected measures on 145 military personnel who were deployed as part of either Operation Iraqi Freedom or Operation Enduring Freedom. We have designed and implemented processing guidelines for imaging, EEG, and clinical data. To date we have found evidence for diffuse white matter abnormalities and reduced coordination of EEG activity in association with blast exposure. We have also developed a tool for systematic classification of head injury from blast when assessed by self-report.

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Introduction

The clinical presentation of individuals with blast-related neural damage and post-traumatic psychopathology are markedly similar and thus a clear description of the direct consequences of explosive blast is complicated by the emotional and cognitive sequelae of psychological trauma. The inability to clearly demonstrate the basis of symptomatology has led to confusion for the soldier and his or her loved ones as well as difficulty prescribing effective treatments and developing interventions that return injured soldiers to adaptive functioning. In the current study, we employ sophisticated measures of neural function and structure to characterize brain injury from explosive blasts in a sample of Operation Iraqi Freedom (OIF) National Guard soldiers who returned from deployment in the fall of 2007. To fully characterize the effects of blast on the brain and differentiate them from post-traumatic stress disorder, we contrast groups of soldiers exposed to blast with groups experiencing post-traumatic stress disorder. The study provides a means for separating co-occurring conditions of brain injury due to explosive blast and post-traumatic psychopathology. Information that clarifies the basis of symptoms in blast-related brain injury and post-traumatic stress disorder will improve diagnostic separation of the two conditions. In summary, this investigation improves the characterization of blast-related traumatic brain injury, describes the essential features of the condition in terms of neural function and structure to inform diagnosis, and characterizes mechanisms of recovery after blast-related neural injury to allow the creation of interventions that return soldiers to maximum levels of functioning.

Body

Based on the proposed statement of work, the following milestones were projected to occur within the second year of the study:

1. **Data for second cohort entered and preprocessed**

Data entry:

During the past year study personnel have augmented a relational database to store data gathered as part of this study. This database is fully functional and we continue to implement a procedure by which data are entered for each participant. All consented participants have demographic, clinical, and biological data entered into the database. All consented participants have data entered on a regular basis shortly after they complete study procedures. Lab personnel have essentially entered all available data to date. Study personnel have been trained in data entry for the database, and processes are in place for checking the accuracy of entered data.

Data processing:

Traumatic Brain Injury (TBI) Consensus: Our research team has met regularly to implement the process by which raters with expertise in the field of neuropsychology and brain injury are able to score severity of brain injury in our participants (see appendix for relevant publication Nelson N.W., Hoelzle J.B., McGuire K.A., Ferrier-Auerbach A.G., Charlesworth M.J., Sponheim S.R. Neuropsychological evaluation of blast-related concussion: Illustrating the challenges and complexities through OEF/OIF case studies. *Brain Injury,* 2011*)* We have created a rating scheme (the Minnesota Blast Exposure Screening Tool [MN-BEST]) and our consensus group of doctoral level neuropsychologists and psychologists meets regularly to determine the categorization of cases.

Mental Health Consensus: Ph.D. level psychologists and advanced doctoral students under supervision by doctoral level staff have been trained to review clinical information to carry out a consensus clinical diagnosis in order to maximize the accuracy and reliability of diagnoses of mental disorders.

Neuroimaging and Electroencephalography (EEG) data: Magnetic resonance imaging and EEG data processing pipelines have been fully developed and have been implemented with data from the second cohort of subjects.

Data storage:

Electronic Data: We have approval from relevant institutional review boards to store data both at the Minneapolis VAMC and at the University of Minnesota. For electronic data, we house most data to be used for data analysis in neuroimaging and EEG data sets and a relational database on servers at the University of Minnesota. Information in all data sets is only accessible by first entering a password to access the secure server, then by entering a second password to access the database. Identifiable information is housed behind the VA firewall. Within the secure VA IT infrastructure study information is stored on a drive that

is accessible only to lab and VA IT personnel. All documents with identifiable participant information on this server are additionally password protected. Data at Minneapolis VAMC and University of Minnesota servers are partially redundant and are regularly backed up by each institution, therefore acquired data is protected from loss.

Hard Copies of Data: We store paper copies of data at the Minneapolis VA in locked filing cabinets within locked offices. We store identifiable information separately from clinical and biological data gathered as part of this study.

2. Complete supplemental analyses to ensure quality of data and review trends

Preliminary analyses reveal that we have successfully enrolled individuals with significant exposure to explosive blasts as well as those suffering from post traumatic stress symptomatology. This permits an examination of how these aspects of contemporary battle impact brain function and structure. Initial analyses of indices of brain structure shows that acquired data to date are of high quality with minimal movement artifacts. Processing of EEG data also reveals high quality high-density EEG recordings with minimal artifact. Group comparisons of structural MRI data reveal sparse and subtle abnormalities in white matter associated with exposure to explosive blast (submitted manuscript: Davenport N.D., Lim K.O., Armstrong M.T., Sponheim S.R. Diffuse and spatially variable white matter disruptions are associated with blast-related mild traumatic brain injury). Analyses of preliminary data also reveal that lower integrity of white matter tracts is related to poor functional synchronization of EEG signals over frontal portions of the brain (see Sponheim S.R., McGuire K.A., Kang S.S., Davenport N.D., Aviyente S., Bernat E.M., Lim K.O. (2011). Evidence of disrupted functional connectivity in the brain after combat-related blast. *Neuroimage, 54 Supplement 1,* S21-9.). Therefore, analyses to date yield trends in support of study hypotheses.

Complete analyses of structural data and EEG-based measures of brain function await collection of data from the remaining to be enrolled participants.

3. Telephone screen to obtain third cohort of 45 subjects

At the end of this year, our goal, as stated on our Statement of Work, was to have obtained a total of 135 participants (45 within this past year). Recruitment of potential participants into our study has been a primary focus of the study. Initially, we had hoped to recruit only participants who had taken part in a sister study and who appeared, based on their responses to this sister study, to be likely to meet inclusion criteria for our study. However, due to low base rates of PTSD, we have continued to expand our recruitment strategies within the past year in an effort to meet our stated goals of eventually obtaining 45 individuals in each of 4 groups: PTSD (PTSD, No Blast Exposure), Blast (Blast Exposure, No PTSD), PTSD and Blast, and Control (neither PTSD nor Blast). We have received approval from all relevant institutional review boards to use multiple strategies. Thus, in the past year, we have recruited participants in the following ways:

1. Recruiting individuals who have taken place in a sister study and who have expressed interest in being contacted for future research.

2. Coordinating with clinical teams at the Minneapolis VA in order to obtain referrals of potential participants who are likely to meet inclusion criteria for our study. This strategy has been implemented in an effort to reach more individuals with symptoms of PTSD and blast-related brain injury.
3. Used lists of potential participants who have received services at the Minneapolis VA and have been diagnosed with PTSD.
4. Contacting the OIF/OEF program at our local VA Medical Center in an effort to broaden our recruitment strategies. Through this program, we have been able to distribute flyers to recently returned service members, as well as establish relationships with clinicians at the Minneapolis VA who might be able to refer potential participants to our study.
5. Screening potential participants who have been referred by word of mouth or by other participants in our study.
6. During this quarter, we have also collaborated with another study to target individuals with combat-related PTSD to increase the number of participants with PTSD in our sample.

After identifying an individual potentially eligible for participation, our recruitment procedure involves sending a letter if the individual has not yet contacted us for study participation. We then follow up with potential participants by calling them to fully determine interest and eligibility for participation. As of the end of this year (as of 3/31/11), we have sent out 583 letters to participants notifying them of our study. In addition, 47 participants have contacted us after being self-referred or referred to our study by another participant or clinical provider. Of those 630 potential participants (those contacted via letter and those who contacted us):

- Number of Participants (out of the participants who were originally sent letters without contacting us first) attempted contact via phone: 583
- Number of Participants not reached via phone (invalid number; never reached by study personnel): 240
- Number of Participants not interested in participating: 101
- Number of Participants excluded for medical history or waitlisted: 156

4. Gather clinical, EEG, and MRI data on 3rd cohort

We have continued to collect data on participants during this quarter at a rate that is consistent with our Statement of Work and exceeds the recruitment goal for the year.

Total Number of participants who gave informed consent for, are currently taking part in, and/or completed the study: **145**

Control Group: 42
Blast Group (Blast Exposure, NO PTSD): 42
PTSD Group (PTSD, No Blast Exposure): 20
Blast and PTSD Group: 41

116 participants have completed all procedures
26 participants have completed some procedures and will not be completing the rest

Since our last annual report (at which time 92 participants had been consented into our study), 53 additional participants have consented to be in our study. We have calculated the rate of participant recruitment necessary in order for us to meet our goal of obtaining the remaining 35 participants over the next year. The rate of recruitment needed to meet our recruitment goals is well within our means.

5. Data for third cohort entered and preprocessed

Over the third year of grant funding we have implemented pipelines for the processing of structural magnetic resonance imaging (MRI) data and EEG recordings. The MRI structural data pipeline includes quality control measures that are employed shortly after data collection to ensure acceptable data quality. The EEG processing pipeline involves visual review of all EEG files gathered from subjects. We have also developed an independent components analysis (ICA) based approach to EEG artifact identification and removal that will facilitate good signal-to-noise in the EEG data. This has proven to be of particular importance when time-frequency analyses are employed to characterize EEG abnormalities that might be associated with blast-related mild traumatic brain injury. Finally, the computational and information technology infrastructure has been expanded and now supports the analysis, integration, and management of complex neuroimaging data.

In the past year, study personnel have continued to fill and use a relational database for the study, which is a sophisticated means of linking different databases so that data pulls can be flexibly carried out and data audits can be efficiently performed. During this past year, full utilization of the database was a priority. Study personnel have also been trained to access data within the database in order to perform data analyses.

Key Research Accomplishments

- As part of this study, we have developed a tool (The Minnesota Blast Exposure Screening Tool [MN-BEST]) to categorize the severity of blast and nonblast head injuries on a continuum (See appendix: Nelson, Hoelzle, McGuire, Ferrier-Auerbach, Charlesworth, & Sponheim, *Brain Injury,* 2011). We are currently examining the reliability and validity of the measure and eventually will disseminate the tool for public use.
- We have found that subtle and spatially diffuse white matter deficits are associated with exposure to blast and that the number of abnormalities increase with more than a single blast exposure (See appendix: submitted paper Davenport N.D., Lim K.O., Armstrong M.T., Sponheim S.R. Diffuse and spatially variable white matter disruptions are associated with blast-related mild traumatic brain injury.)
- We have found that diminished functional coordination of EEG activity over frontal brain regions after blast exposure is associated with reduced integrity of white matter tracts the innervate the frontal lobes of the brain (See appendix: Sponheim S.R., McGuire K.A., Kang S.S., Davenport N.D., Aviyente S., Bernat E.M., Lim K.O., *Neuroimage,* 2011.) We are currently testing this association for replication in newly collected data as part of the present project.
- We have established a researcher guided system for applying independent component analysis (ICA) to EEG data in order to effectively eliminate environmental and bio-electrical artifacts from the signals.
- As an overarching goal of the study, we expect that as a result of this research, both researchers and clinicians will be able to better differentiate between PTSD and mild TBI due to blast. It is difficult to clinically differentiate between the two disorders because their presentations are similar and no biological markers are available to inform the distinctions between the two conditions. Additionally, the diagnosis of nonimpact blast-related mild TBI is not without controversy. Our research is intended to clarify differences between the two conditions, and thus lead to better treatment of the disorders.

Reportable Outcomes

Publications

1. Sponheim S.R., McGuire K.A., Kang S.S., Davenport N.D., Aviyente S., Bernat E.M., Lim K.O. (2011). Evidence of disrupted functional connectivity in the brain after combat-related blast. *Neuroimage, 54* Supplement 1, S21-9

2. Nelson N.W., Hoelzle J.B., McGuire K.A., Ferrier-Auerbach A.G., Charlesworth M.J., Sponheim S.R. (in press). Neuropsychological evaluation of blast-related concussion: Illustrating the challenges and complexities through OEF/OIF case studies. *Brain Injury, 25*, 511-25

3. Nelson, N. W., Hoelzle, J. B., McGuire, K. A., Ferrier-Auerbach, A. G., Charlesworth, M. J., & Sponheim, S. R. (2010). Evaluation context impacts neuropsychological performance of OEF/OIF veterans with reported combat-related concussion. *Archives of Clinical Neuropsychology*, 25, 713-23.

4. Nelson N.W., Hoelzle J.B., McGuire K.A., Sim A.H., Goldman D.J., Ferrier-Auerbach A.G., Charlesworth M.J., Arbisi P.A., Sponheim S.R. (in press). Self-report of psychological function among OEF/OIF personnel who also report combat-related concussion. *The Clinical Neuropsychologist*.

Submitted Publications

1. Davenport N.D., Lim K.O., Armstrong M.T., Sponheim S.R. (submitted). Diffuse and spatially variable white matter disruptions are associated with blast-related mild traumatic brain injury.

Presentations

1. Hoelzle, J., Nelson, N., McGuire, K., Ferrier-Auerbach, A., Charlesworth, M., Doane, B., & Sponheim, SR (February, 2011). Factor analysis of cognitive and psychological response validity measures in a sample of U.S. veterans. Presented at the 39th Annual Meeting of the International Neuropsychological Society in Boston, Massachusetts.

2. McGuire K.A., Nelson N.W., Hoelzle J.B., Ferrier-Auerbach A.G., Charlesworth M.J., Armstrong M., Sponheim S.R. (June, 2010). Persistent Postconcussive Symptoms and PTSD in OEF/OIF Military Personnel. Presented at the annual meeting of the American Academy of Clinical Neuropsychology (AACN). Chicago, Illinois.

3. Nelson, N.W., Hoelzle, J. B., McGuire, K. A., Ferrier-Auerbach, A. G., & Charlesworth, M. J., & Sponheim, S. R. (June, 2010). Predictors of neuropsychological dysfunction among veterans of Operation Iraqi Freedom (OIF). Presented at the annual meeting of the American Academy of Clinical Neuropsychology (AACN). Chicago, Illinois.

4. Nelson, N. W., Hoelzle, J. B., McGuire, K. A., Ferrier-Auerbach, A. G., & Charlesworth, M. J., & Sponheim, S. R. (June, 2010). The Minnesota blast exposure screening tool

(MN-BEST): Introducing a systematic investigatory approach to blast exposure and concussion in Veterans of Operation Iraqi Freedom (OIF). Presented at the annual meeting of the American Academy of Clinical Neuropsychology (AACN). Chicago, Illinois.

5. Nelson, N. W., Hoelzle, J. B., McGuire, K. A., Sim, A. H., Goldman, D., Ferrier-Auerbach, A. G., & Charlesworth, M. J., Arbisi, P. A., & Sponheim, S. R. (June, 2010). Context matters: Examination of MMPI-2 and MMPI-2-RF validity scales among OEF/OIF veterans evaluated in forensic, clinical, and research settings. Presented at the annual meeting of the American Academy of Clinical Neuropsychology (AACN). Chicago, Illinois.

Conclusion

The major accomplishments of the first year were to establish methods of data collection and recruitment and to begin to recruit participants into our study. This entailed obtaining permissions from relevant institutional review boards. During the second year of grant funding, we have continued to recruit participants in a manner consistent with our Statement of Work. Now in the third year we have continued collecting clinical, EEG, and MRI data on consented participants. To date we continue to be on schedule for the number of participants enrolled in the study. We continue with data entry and processing according to guidelines we established in the last two years, thus ensuring that we have completed all tasks in a manner consistent with our Statement of Work for the third year of the study. We have calculated the rates of data collection necessary to complete data collection on approximately 35 remaining participants (for a study total of 180 participants) prior to the end of the project. Given the remaining 6 months in which we would like to collect data, we have calculated that we will need approximately six clinical visits per month, which will entail needing to perform phone screens on at least twice that many people per month. This data collection plan is well within our means, and we are confident that this plan will allow us to reach our goal of obtaining complete data within the allotted study period.

The significance of progress to date (i.e., “so what”) is that we have a well specified procedure for classifying blast injury based on self report which will enhance the accuracy of classification of blast-related TBI in clinics and medical centers. We also have preliminary evidence that both the phase synchronization of the EEG and the integrity of white matter structures in the brain may inform a diagnosis of blast-related mild TBI.

We expect that data collected as part of this study will add to what is known about alterations in brain function and structure associated with exposure to blasts in battle. Inclusion of a group of subjects affected by post-traumatic stress symptomatology from battle allows the differentiation of the emotional consequences of explosions from the effects of the blast-related pressure wave. Identification of brain abnormalities unique to each condition (blast-related TBI and post-traumatic stress) will help clinicians and researchers accurately assess conditions evident in soldiers exposed to explosions. Such knowledge will also inform the design of treatments that return the injured to optimal levels of functioning. The results of this study may also help military leadership and health care professionals prescribe treatments that are personalized to an individual's underlying brain pathology.

References

1. Nelson N.W., Hoelzle J.B., McGuire K.A., Ferrier-Auerbach A.G., Charlesworth M.J., Sponheim S.R. (in press). Neuropsychological evaluation of blast-related concussion: Illustrating the challenges and complexities through OEF/OIF case studies. *Brain Injury, 25*, 511-25

2. Davenport N.D., Lim K.O., Armstrong M.T., Sponheim S.R. (submitted). Diffuse and spatially variable white matter disruptions are associated with blast-related mild traumatic brain injury.

3. Sponheim S.R., McGuire K.A., Kang S.S., Davenport N.D., Aviyente S., Bernat E.M., Lim K.O. (2011). Evidence of disrupted functional connectivity in the brain after combat-related blast. *Neuroimage, 54* Supplement 1, S21-9

Appendices

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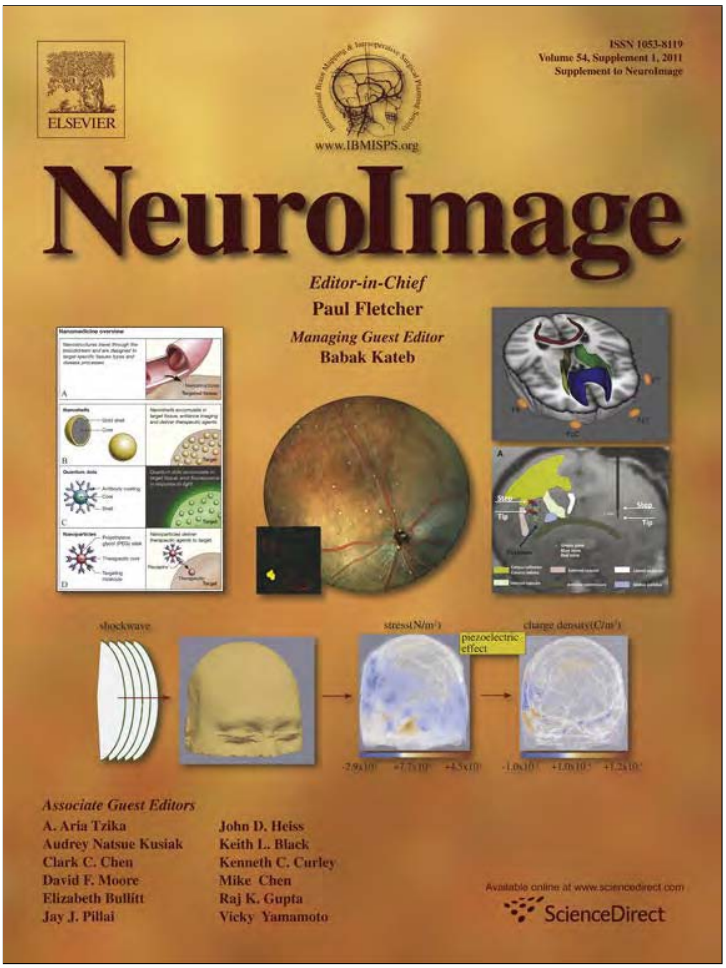

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Evidence of disrupted functional connectivity in the brain after combat-related blast injury

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ABSTRACT

Non-impact blast-related mild traumatic brain injury (mTBI) appears to be present in soldiers returning from deployments to Afghanistan and Iraq. Although mTBI typically results in cognitive deficits that last less than a month, there is evidence that disrupted coordination of brain activity can persist for at least several months following injury (Thatcher et al., 1989, 2001). In the present study we examined whether neural communication may be affected in soldiers months after blast-related mTBI, and whether coordination of neural function is associated with underlying white matter integrity. The investigation included an application of a new time–frequency based method for measuring electroencephalogram (EEG) phase synchronization (Aviyente et al., 2010) as well as fractional anisotropy measures of axonal tracts derived from diffusion tensor imaging (DTI). Nine soldiers who incurred a blast-related mTBI during deployments to Afghanistan or Iraq were compared with eight demographically similar control subjects. Despite an absence of cognitive deficits, the blast-related mTBI group exhibited diminished EEG phase synchrony of lateral frontal sites with contralateral frontal brain regions suggesting diminished interhemispheric coordination of brain activity as a result of blast injury. For blast injured (i.e., blast-related mTBI) soldiers we found that EEG phase synchrony was associated with the structural integrity of white matter tracts of the frontal lobe (left anterior thalamic radiations and the forceps minor including the anterior corpus callosum). Analyses revealed that diminished EEG phase synchrony was not the consequence of combat-stress symptoms (e.g., post-traumatic stress and depression) and commonly prescribed medications. Results provide evidence for poor coordination of frontal neural function after blast injury that may be the consequence of damaged anterior white matter tracts.

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Introduction

Injury from explosive blast is a prominent feature of contemporary combat (DePalma et al., 2005). Although protective armor and acute medical intervention allow soldiers to survive explosions, a growing number of veterans will have disability stemming from blast-related brain damage (Warden, 2006). Estimates of the prevalence of blast-induced brain injury vary (Carlson et al., 2010) but a study employing clinician assessments and informant reports indicated that about a fifth of individuals in a Brigade Combat Team sustained traumatic brain injuries due to blast during a 1-year deployment to the Iraq War (Terrio et al., 2009). To date, few studies have systematically investigated the effects of blast injury on brain function and the well-being of soldiers (Ling et al., 2009; Taber et al., 2006). There is evidence that survivors of blasts on the battlefield have mostly incurred mild traumatic brain injury (mTBI) (Belanger et al., 2009; Hoge et al., 2008; McCrea et al., 2008; Schneiderman et al., 2008). The predominance of mTBI in returning soldiers from wars may be due to the fatal nature of explosive blasts with more powerful pressure waves (e.g., 56 to 76 psi) that hemorrhage air-filled organs (e.g., lung) and cause death (see DePalma et al., 2005; Mayorga, 1997; Wolf et al., 2009 for reviews). Thus, there is a limit to the wave strength that impacts the brain in soldiers who survive the explosion. Recent modeling of explosive blasts has provided evidence that a pressure wave resulting in 50% mortality due to damage to the lung results in head injury approximately equivalent to that of an mTBI associated with sports concussion (Moore et al., 2009). In the present study we sought to use quantitative analyses of resting state electroencephalograms (EEGs) to characterize the effects of explosive blast on soldiers who were deployed to conflicts in Afghanistan and Iraq. Because

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diffuse axonal injury and the resulting disruption in neural communication are thought to be primary effects of blast-related mTBI (Taber et al., 2006), we were specifically interested in whether deficient functional synchronization of EEG activity was evident in soldiers who had experienced explosive blasts perhaps reflecting compromised connective fibers that support communication between brain regions.

mTBI (i.e., concussion) typically results in cognitive deficits immediately after the brain injury (Barr and McCrea, 2001); however impairment appears to be short-lived and nearly undetectable a month post injury (see McCrea et al., 2009 for a review). A recent systematic and detailed analysis concluded that mTBI resulted in essentially no cognitive impairment on neuropsychological indices 3 months after injury (Belanger et al., 2005). Yet, it is an open question whether mTBI due to explosive blast is unique and results in behavioral, cognitive, and emotional disruption that is distinct from other mTBIs (e.g., sports concussion). An initial study has provided evidence that the cognitive sequelae of blast injury is essentially the same as that of other mTBIs, and that what is most predictive of longer terms cognitive deficits from brain injury is injury severity and not mechanism of injury (Belanger et al., 2009). Because the brain can adapt and compensate for damage, and assessment of cognitive functions is largely determined through behavior, neuropsychological evaluation may fail to capture phenomena that characterize neural damage. In an initial effort to identify the effects of blast-related mTBI we applied direct measures of neural function and structure to a sample of veterans of combat in Iraq and Afghanistan who were injured by explosive blast.

To date there have been only a handful of studies specifically examining the effects of explosive blast on the human brain. Clinical EEG readings of blast injured individuals have been found to be similar to those of individuals who incurred other forms of closed-head injury (Cramer et al., 1949; Fabing, 1947). A more recent EEG study of older veterans who reported blast-exposure predominantly as part of World War II and conflicts in Korea and Vietnam revealed higher scores on a EEG-based discriminant index designed for identification of mTBI (Trudeau et al., 1998). The discriminant index was defined most strongly by abnormalities in EEG phase coherence over frontal brain regions consistent with axonal injury in these areas (Thatcher et al., 1989). Studies of animals have revealed blast-related cognitive dysfunction (Cernak et al., 2001) and depressed EEG signals (Axelsson et al., 2000). Post-mortem and experimental animal studies document white matter hemorrhages, degeneration of nissl bodies, microglial activation, and diffuse axonal injury after exposure to explosive blasts (Kaur et al., 1995, 1997a,b; Svetlov et al., 2009). The evidence suggests that diffuse injury to axons results from high velocity impact of any origin and involves widespread damage to the brainstem, cerebellum, corpus callosum, and parasagittal white matter of the cortex (Meythaler et al., 2001). But the most direct effects of blast injury on the connective fibers of the brain are thought to occur in the corpus callosum, the corticomedullary junction, and frontotemporal areas (Taber et al., 2006) and thus may affect interhemispheric neural communication involving frontal brain regions. Recent advances in computational techniques for analysis of functional magnetic resonance imaging data, magneto-encephalography, and electroencephalographic data have allowed examination of the dynamic synchronization of neural activity across brain regions (Bullmore and Sporns, 2009; Georgopoulos et al., 2007). The functional consequence of blast-related disruption of connective fibers in the brain may well be expressed in terms of poorly coordinated activity across neural structures that is measured through examining the phase synchronization of neural signals (Aviyente et al., 2010; Lachaux et al., 1999).

Individuals who have suffered a mTBI by any mechanism are often found to have normal generalized neuropsychological function and clinical EEGs (Nuwer et al., 2005); however quantitative analysis of EEG data has yielded indices of frequency power, synchrony between brain regions, and asymmetry that can discriminate individuals with mTBI from individuals without brain trauma months after injury (Thatcher et al., 1989). mTBI has also been associated with diminished and delayed event-related potentials in the EEG (Gaetz et al., 2000; Gaetz and Weinberg, 2000; Solbakk et al., 2005) and anomalous time–frequency EEG profiles (Slobounov et al., 2002). Therefore, it appears that direct measures of neural function may be sensitive to the effects of mTBI while behavioral measures of cognitive performance may fail to capture altered brain function due to the injury.

Because of prior evidence for disruption of synchronization in frontal brain activity following mTBI (Thatcher et al., 1989, 2001) we examined whether frontal interhemispheric neural communication may be affected in subjects with mTBI after blast injury and whether interhemispheric coordination of neural function was associated with underlying white matter integrity. To this end, we collected resting state EEG and diffusion tensor imaging data from 9 veterans with blast-related mTBI and 8 demographically similar control subjects. The similarity in the phase of EEG signals from distant electrodes was analyzed as an index of functional synchronization, while fractional anisotropy (FA) of white matter tracts was analyzed as a measure of structural connectivity (i.e., white matter integrity). Because the frontal temporal brain regions appear vulnerable to the effects of blast injury (Taber et al., 2006), we examined interhemispheric phase synchrony of fronto-temporal scalp electrodes (i.e., sites F7 and F8) with several contralateral electrodes. Unique aspects of the analysis included the first systematic application of a new time–frequency based method for measuring phase synchronization (Aviyente et al., 2010) and examination of the relationship between the functional synchronization and structural connectivity of the human brain after exposure to explosive blast.

Method

Participant Characteristics

Nine individuals who had been exposed to explosive blasts during military deployments to Afghanistan or Iraq were compared with 8 healthy controls of similar age and gender. Individuals in the blast injured group were recruited from the Traumatic Brain Injury/Polytrauma clinic at the Veterans Affairs Medical Center in Minneapolis, Minnesota. Recruitment letters were sent to individuals who had recently been referred through the clinic for neuropsychological evaluations. Participants from the control group were recruited through internet advertisements (e.g., Craig's List) and were not necessarily veterans and had not been deployed. Interested individuals were screened through a telephone interview prior to enrollment. Exclusion criteria for all subjects were contraindications to MRI scan, age under 18 or over 60, current medical-condition-related or substance-induced psychotic disorder, alcohol or substance abuse in the past month, severe neurological or psychiatric illness, significant risk of homicide or suicide, current major depressive episode, and an unstable medical condition affecting brain function. Controls were additionally excluded if they had a history of an affective disorder, alcohol or substance dependence, any use of psychotropic medication, moderate to severe brain injury, or concussions with reported effects lasting over 24 h. All subjects were male and Caucasian. Please refer to Table 1 for a summary of participant characteristics and supplemental materials for additional details. The Institutional Review Boards for the Minneapolis VA Medical Center and University of Minnesota approved the study protocol and determined that the investigational procedures were in compliance with the Health Insurance Portability and Accountability Act (HIPAA).

Background and blast-related information was obtained through questionnaires and a review of medical records. Table 2 includes descriptions of the most significant and clearly described explosive

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Table 1
Characteristics of participants.

	Blast group	Controls		
	$N=9$	$N=8$	*t*-Test	
Variable	Mean (SD)	Mean (SD)	Statistic (*df*)	*p* Value
Age (years)	33.7 (7.67)	30.3 (8.00)	0.90 (15)	n.s.
Percent male	100	100	N/A	N/A
Handedness (R/L)	7/2	7/1	N/A	N/A
Years of education	13.7 (1.00)	14.6 (1.92)	1.27 (15)	n.s.
Estimated IQ[a]	112 (13.70)	115 (13.89)	0.49 (14)	n.s.
NSI total score	31.1 (16.59)	5.9 (8.08)	4.06 (15)	0.002
PCL-C total score	42.7 (17.49)	21.1 (4.02)	3.59 (15)	.006
BDI-II total score	14.2 (9.78)	2.3 (2.61)	3.53 (15)	.006

Note. SD = Standard Deviation. IQ = Intelligence Quotient. Estimated IQ was derived from the tables in Jeyakumar et al. (2004) using Vocabulary and Block Design subtests. NSI = Neurobehavioral Symptom Inventory. PCL-C = Posttraumatic Stress Disorder Checklist-Civilian version. BDI-II = Beck Depression Inventory, second edition. Analyses were adjusted for unequal variances when indicated.
[a] Analyses completed on only 8 participants in the blast group.

blasts experienced by subjects. Subjects were classified as blast-injured through reference to the Diagnostic criteria for Mild TBI by the American Congress of Rehabilitation Medicine Special Interest Group on Mild Traumatic Brain Injury and the concussion grading system by the American Academy of Neurology (both reported in Ruff et al., 2009) All blast injured subjects were exposed to blasts that threw them, significantly damaged or threw heavy military vehicles they were riding in, or injured the occupants of the vehicle. All individuals in the blast group had been deployed to either Iraq or Afghanistan and had been exposed to at least one blast explosion. Four individuals were exposed to greater than one explosion (ranging from 2 to 40). Four individuals also reported receiving blows to the head as the result of either their person or their vehicle being displaced by the blast. Estimated mean number of months since the blast injury was 32.7 (SD = 9.26).

Subjects completed a battery of neuropsychological tests designed to assess memory and executive functions. The age-adjusted scaled score of WAIS-III Vocabulary and WAIS-III Block Design also were used to calculate an estimated IQ score. Please see supplemental information for a detailed description of the neuropsychological assessment. Research staff were not blind to group membership of subjects. Subjects also completed questionnaires for the assessment of symptoms following mild brain injury (Neurobehavioral Symptom Inventory [NSI]; Cicerone and Kalmar, 1995), current depressive symptomatology (Beck Depression Inventory-Second Edition [BDI-II]; Beck et al., 1996), and post-traumatic stress symptomatology (Post-traumatic Stress Disorder Checklist-Civilian version [PCL-C]; Weathers et al., 1991).

Electrophysiological data collection and preprocessing

Electroencephalograms (EEG) were recorded using a 64-channel Biosemi Active Two EEG system (http://www.biosemi.com) while subjects were at rest with eyes closed. Electrodes were embedded in an elastic cap and placed on the head to conform to 10-10 nomenclature. Vertical electro-oculograms (VEOG) recorded from above and below the right eye and horizontal electro-oculograms (HEOG) recorded from outer ocular canthi were used to measure eye-movements. EEG signals were digitized at a rate of 512 Hz with 0.5 Hz low frequency and a 60-Hz notch filters. Following data collection, recordings from scalp sites were re-referenced to linked earlobes. Segments of EEG with obvious non-neurogenic signals were deleted after visual inspection aided by amplitude threshold criterion applied to each electrode signal. Brief time periods of non-neurogenic noise in one or two electrodes were interpolated from adjacent electrode signals using spherical spline interpolation (Perrin et al., 1989). Independent component analysis (ICA) using FastICA algorithm (Hyvarinen and Oja, 2000) was then applied to eliminate artifacts from eye-movements, cardiac and muscle activity, and other non-neurogenic sources. Prior to the ICA, principal component analysis (PCA) was applied to the covariance matrix of EEG signals to reduce the number of independent components (ICs). Principal components were retained to account for more than 99.5% of the variance in the original data. ICA was then applied to the reconstituted signals and all resulting ICs were carefully inspected in terms of their topography, frequency power spectrum, and time course. ICs showing

Table 2
Descriptions of blast events and subsequent post-concussive symptoms.

Subject	Blast event	Reported symptoms	LOC	PTA
1	A rocket propelled grenade exploded 20 yards away and the blast wave threw the subject against a barrier.	Disorientation (several seconds), momentarily dazed.	None	None
2	IED detonated on passenger side while subject was driving a truck. Vehicle was armored and engulfed in a ball of flames. Penetrating shrapnel in extremities.	Ongoing tinnitus, described by others as confused for several minutes.	None	None
3	1) Mortar round detonated 10 feet away from subject behind a barrier. Felt pressure wave and was stunned.	(1) Tinnitus, sensitivity to light and noise.	(1) None	(1) Possibly 1 min
	2) IED detonated approximately 16 meters away and the vehicle was thrown up onto two wheels.	(2) Tinnitus	(2) None	(2) None
4	Subject was a passenger in an 8-ton armored vehicle that ran over a land mine and was thrown into the air.	Headache, tinnitus, nauseous for 24 to 36 h, blurred vision, tingling in legs, poor coordination for 3 h.	Yes, for unknown period	None
5	Subject was a gunner in a Humvee that was hit by an IED detonation followed by a mortar blast. Blast wave forced his body against the inner walls of the vehicle.	Headache, tinnitus, blurred vision, impaired concentration.	None	Yes, for unknown period
6	Subject was a gunner in a Humvee that swerved when an IED was detonated. Shrapnel was lodged in his helmet and sunglasses. Subject was thrown around in the turret.	Tinnitus, slightly stunned, medic said he was okay to return to duty.	None	None
7	Subject was in vehicle that drove over a mine in order to detonate it. Blast propelled the subject upward in the vehicle.	Headache, tinnitus.	5 s	None
8	Subject was in vehicle that was hit by an IED. Others in the vehicle were injured.	Headache, dazed for several minutes, tinnitus for a few days, hearing loss on right side.	Unknown	None
9	Subject was in a vehicle that was attacked. 28 IED's were detonated within 2 ft of the vehicle over a 3-h period.	Headache, dazed and confused for 15 min.	None	None

LOC—loss of consciousness; PTA—post-traumatic amnesia; IED—improvised explosive device; Humvee—High Mobility Multipurpose Wheeled Vehicle.

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high temporal correlations with VEOG or HEOG signals and typical topography of high frontal polar activity were identified as eye-movement artifacts. ICs characterized by pattern of periodic deflections in the component time series, persistent activity throughout the recordings, low-frequency (<3 Hz) peak power spectrum, and a unilateral or bilateral posterior topography were identified as cardiac artifacts. Muscle artifacts were characterized by spectra with broad peak from 20 to greater than 60 Hz, topography showing prominent activity restricted to marginal electrodes close to facial muscles, and periods of high frequency activations (McMenamin et al., 2010). Brief periods of muscle artifact were removed (i.e., less than 1/5 of the entire time-series), while longer periods of muscle artifact characterized by ICs were removed through elimination of the IC from the reconstituted signal. After preprocessing with ICA and artifact removal, EEG recordings were reconstituted from the remaining ICs, subsampled to 128 Hz, and segmented into 4-s epochs with 50% of adjacent segments.

EEG phase synchrony analysis

Time-varying complex energy time frequency distribution (TFD) of all the epoched EEG signals were obtained using a recently introduced method employing the reduced interference distribution (RID) Rihaczek distribution (Aviyente et al., 2010). The RID-Rihaczek distribution computes a complex TFD with uniform time–frequency resolution, avoiding the trade-off between time and frequency resolution inherent to wavelet analysis. In the present analyses we defined a high resolution complex TFD of all epochs of the EEG signals, the phase spectrum of the signals and the phase differences between two electrode signals were computed. To avoid spurious phase synchrony between scalp electrodes due to volume conduction (Srinivasan et al., 2007), only electrodes more than 12 cm apart were selected and used for phase synchrony estimation. Phase-synchrony was computed using a phase locking value (PLV) (Lachaux et al., 1999) which represented the average difference in phase-synchrony between a pair of electrodes across epochs. The PLV is normalized so that values near 1 indicate highly similar phase between electrodes across trials and values near 0 indicate almost entirely unrelated phase between electrodes across trials. Thus, PLV was used to quantify the synchrony between EEG signals of distant electrode pairs independently for each time–frequency point on the TFD. To compute EEG phase synchrony for various frequency bands, PLVs in delta (1–3 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta-1 (13–20 Hz), beta-2 (21–30 Hz), and gamma (31–64 Hz) ranges were averaged. To compare the average PLVs between subjects with mTBI and control subjects, non-parametric Wilcoxon ranksum tests were conducted for the phase synchrony indices of pairs of distant electrodes in all frequency bands.

DTI acquisition and processing

Diffusion weighted images were acquired on a 1.5T Philips Achieva (Andover, MA, USA) scanner using a multichannel head coil. Head movement was minimized by placing cushions around the participant's head. A 3-plane localizer was used for orientation and prescription of 3D scans. Diffusion weighted images were collected with a single-shot spin echo planar diffusion sequence of 55 axial slices covering the entire cerebrum and as much of the cerebellum as possible. Thirty-three images were collected at each slice location, 32 of which had diffusion gradients applied in non-collinear direction with $b = 800$ s/mm^2 msocom2 and one with no diffusion gradient ($b = 0$). Additional acquisition parameters for the diffusion sequence were: TR = 7200 ms, TE = 80 ms, Flip Angle = 90 deg. Acquisition voxel size was $2.14 \times 2.14 \times 2.5$ mm^3.

The diffusion weighted images were corrected for eddy current distortions, and fractional anisotropy (FA) values were calculated at each brain voxel using FSL software (Smith et al., 2004) Each FA map was nonlinearly registered to a standard FA image (Mori et al., 2005), and the inverse of this transformation was used to register regions of interest (ROIs) defined in that standard space (Hua et al., 2008; McCrea et al., 2009) back to each subject's space. Four of these ROIs were chosen for the current analysis: forceps major (posterior corpus callosum), forceps minor (anterior corpus callosum), left anterior thalamic radiations, and right anterior thalamic radiations. These regions are shown in Fig. 3. FA values of voxels contained within each ROI were averaged.

Results

Clinical and cognitive characteristics of blast injured and control samples

Blast and control groups were of similar age, gender composition, handedness, educational backgrounds, and intelligence (see Table 1). The

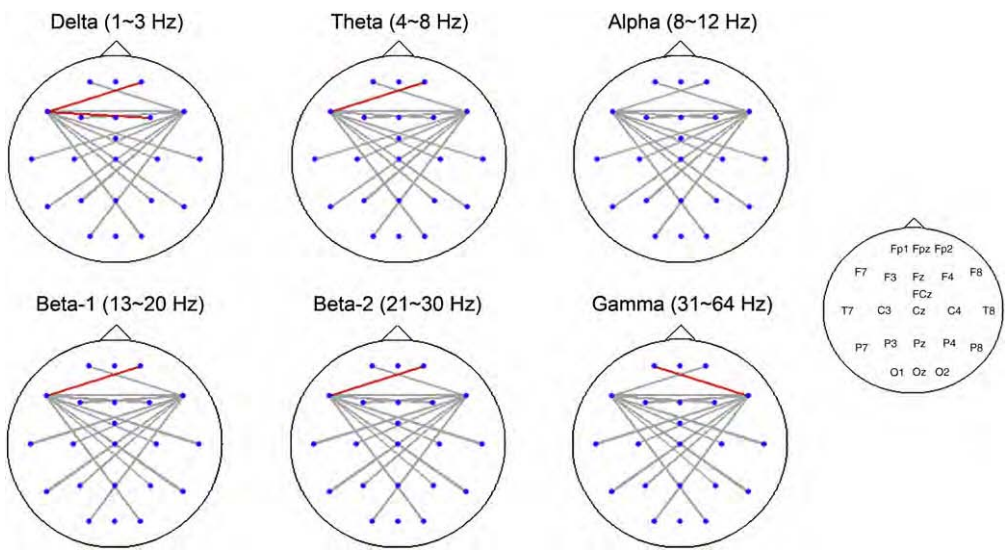

Fig. 1. Topographical representation of EEG phase synchrony results for comparisons of blast-related mTBI and control groups. Phase synchrony was computed for 15 interhemispheric electrode pairings (gray and red lines) involving lateral frontal scalp electrodes (i.e., F7 and F8) in six frequency bands. Red lines indicate a tendency for blast-related mTBI subjects to show reduced phase synchrony between sites ($p < 0.05$).

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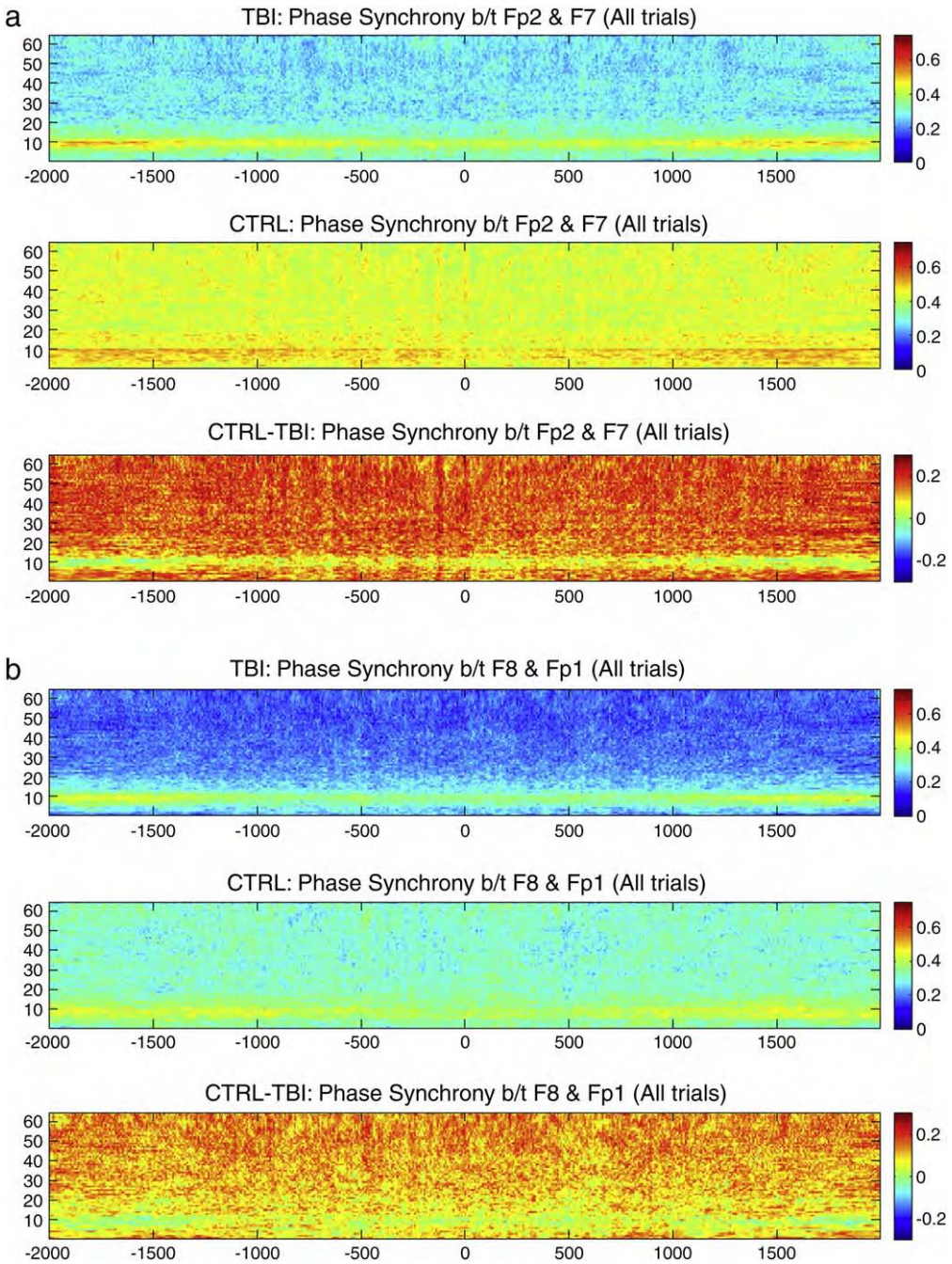

Fig. 2. Average EEG phase synchrony surfaces for blast-related mTBI (TBI) and control groups for 4-s resting state epochs (i.e., trials). *x*-Axis is time in milliseconds with "0" representing the midpoint of the epoch, *y*-axis is frequency (Hz), colors represent between electrode phase synchrony values or their difference (CTRL-TBI). (a) Phase synchrony between the left lateral frontal (F7) and right orbital frontal (Fp2) regions, and (b) the same for right lateral frontal (F8) and left orbital frontal (Fp1) regions. Note diminished phase synchrony in the blast-injured mTBI group for most frequencies with the exception of the alpha band (10 Hz).

blast exposed group had elevated levels of current postconcussive symptoms as measured by the NSI, moderate levels of post-traumatic stress symptomatology but on average below the commonly used PCL-C cut-off for a diagnosis of post-traumatic stress disorder, and mild levels of depressive symptomatology on the BDI-II. The control group had lower scores than the blast injured group on the NSI, PCL-C, and BDI-II. Analysis of cognitive functioning in the blast injured group using a repeated-measures ANOVA with group (blast injured, control) as between subjects factor and neuropsychological index as a within subject factor of primary neuropsychological indices (see Supplemental Table 1 for listing) failed to reveal a group main effect ($F_{1,13} = 0.03$, ns) or an interaction of group and index ($F_{16,208} = 0.51$, ns). Exploratory univariate analyses also failed to reveal differences between the blast injured and control groups on any neuropsychological index, consistent with mTBI due to blast injury not resulting in enduring measurable cognitive dysfunction.

Between region synchronization of functional brain activity: EEG phase locking

Preliminary analyses of group differences in EEG phase synchrony between distant electrodes revealed diminished phase locking in the blast injured group over anterior portions of the brain and only between

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regions of opposite cerebral hemispheres. The two most affected sites resided over homologous regions of the lateral prefrontal cortex (F7, F8). To more fully examine the pattern of diminished EEG synchronization involving the lateral prefrontal electrode sites we tested the hypothesis that blast injury caused inter-hemispheric communication dysfunction involving lateral frontal cortex by specifically testing for group effects in phase locking between each lateral frontal site (F7, F8) and eight electrodes distributed across the opposite cerebral hemisphere. Compared to the control group, the blast injured group showed a tendency toward reduced interhemispheric EEG phase synchrony between frontal sites (see Fig. 1). Blast injured individuals showed diminished EEG synchrony between the left lateral frontal electrode site (F7) and the right orbital frontal electrode (Fp2) for several frequency bands (Cohen's d used to represent effect size) (delta: $p<.05$, $d=1.19$; theta: $p<.05$, $d=1.07$; beta-1: $p<.05$, $d=1.06$; beta-2: $p<.05$, $d=1.20$), and right lateral electrode (F4) in delta ($p<.05$, $d=1.00$). The blast injured group also had diminished reduced EEG synchrony between the right lateral frontal electrode (F8) and the left orbital frontal electrode (Fp1) for gamma frequencies ($p<.05$, $d=.92$). Fig. 2 depicts the phase synchrony surfaces for locking values for the blast mTBI and control groups between F7 and Fp2 and between F8 and Fp1. Although the pattern of group differences generally replicated across electrodes, frequency bands, and both lateral frontal electrode sites, the probability of Type I error cannot be ignored given group comparisons over 15 electrode pairs and 6 frequency bands, thus findings suggest only a tendency toward interhemispheric communication reduction in subjects with blast-related mTBI.

Poor synchronization of brain function after blast and white matter structures: association between EEG phase locking and DTI fractional anisotropy (FA)

To test whether the interhemispheric frontal phase synchrony decrement noted in the blast injured group was associated with the integrity of white matter structures thought to be affected in brain injury, we computed Pearson correlations for the frontal interhemispheric functional connectivity EEG indices with the mean fractional anisotropy (FA) of four major white matter tracts related to frontal interhemispheric communication: forceps major, forceps minor, and the right and left anterior thalamic radiations. Fig. 3 depicts the tracts characterized in the analysis. To control for multiple comparisons the criterion p-value was set at .0028. FA of the forceps minor in blast injured subjects was associated with beta-2 frequency phase synchrony between F7 and Fp2 electrode pairs ($r=0.91$, $p=0.002$). FA of the left anterior thalamic radiations in blast injured subjects was also associated with beta-2 frequency phase synchrony between F7 and F4 ($r=0.90$, $p=0.003$) and between F8 and F3 ($r=0.92$, $p=0.001$), as well as for gamma frequency phase synchrony between F8 and F3 ($r=0.91$, $p=0.002$). There were no associations between EEG synchronization indices and measures of integrity of frontal interhemispheric white matter tracts in the control group. Fig. 4 presents scattergrams depicting the four significant associations in the blast injured group and the absence of associations in the control group. The pattern of neural function–structure associations in the blast injured group provides evidence for poor functional synchronization of frontal brain regions after blast-related mTBI being attributable to the structural integrity of white matter tracts serving the frontal lobes. Blast injured and control groups failed to differ in the fractional anisotropy for the four tracts of interest (all t's<1.44 and all p's>0.2) suggesting that although explosive blast may compromise white matter tracts, the disruption is more sensitively detected through the use of EEG phase synchrony measures.

EEG phase locking and demographic, clinical and cognitive characteristics

We conducted a set of statistical tests to determine whether diminished inter-hemispheric functional synchrony was associated with the demographic, clinical or cognitive status of subjects. Supplemental materials detail these ancillary analyses. EEG phase synchrony measures failed to be associated with age and the NSI, BDI-II, and PCL-C suggesting that self-reports on these symptom questionnaires do not reflect direct neural consequences of mTBI due to blast injury. Within the blast injured group a clinician-based diagnosis of post-traumatic stress disorder (PTSD) and prescribed antidepressant or sleep medication were associated with only greater EEG phase synchrony in select bands and frequencies that were different from those associated with blast mTBI, thus demonstrating that psychopathology or treatment did not result in the blast-related decrement in EEG phase synchrony. Similarly, diminished EEG phase synchrony was not associated with poorer neuropsychological performance. In addition to cognitive recovery typically occurring within a month of mTBI, it is possible that because EEG data were gathered during an eye's closed resting state the identified phase synchrony abnormalities are associated with a tonic brain state and are unrelated to active brain states elicited by neuropsychological tasks.

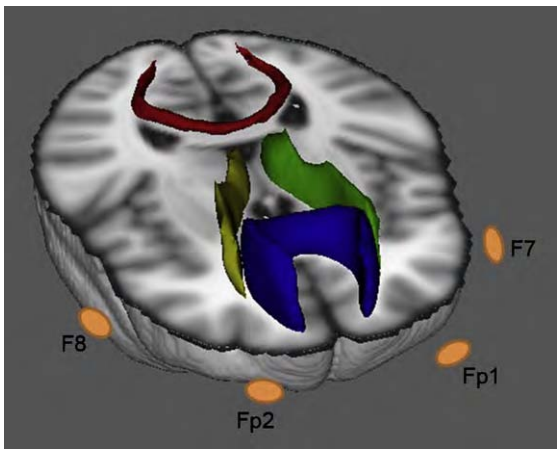

Fig. 3. Four white matter tract regions of interest (ROIs) were chosen for the current analysis: forceps major (red), forceps minor (blue), left anterior thalamic radiations (green), and right anterior thalamic radiations (yellow). Approximate positions for electrodes at F8, Fp2, Fp1, and F7 that demonstrated decreased EEG phase synchronization in the blast-related mTBI group are shown relative to tract-based ROIs. Only the three anterior tract ROIs and not the forceps major were associated with decreased EEG phase synchrony in blast-related mTBI soldiers.

Conclusions

In the present study we applied a novel time–frequency based method (Aviyente et al., 2010) for characterizing synchronization of EEG signals gathered from blast injured soldiers and demographically similar control subjects. Despite an absence of deficits on neuropsychological indices, the blast injured group exhibited diminished EEG phase synchrony of lateral frontal sites with contralateral frontal brain regions suggesting diminished interhemispheric coordination of brain activity as a result of blast injury. For soldiers who had mild TBI as a result of explosive blasts we found that the EEG phase synchrony of lateral frontal electrodes with frontal regions of the opposite cerebral hemisphere was associated with measures of white matter structural integrity (fractional anisotropy) of frontal white matter tracts (forceps minor and anterior thalamic radiation) but not an interhemispheric white matter tract in posterior brain regions (forceps major). Thus, the present analysis yielded evidence for frontal axonal tract structural integrity correlating with poor synchronization of neural function after blast injury.

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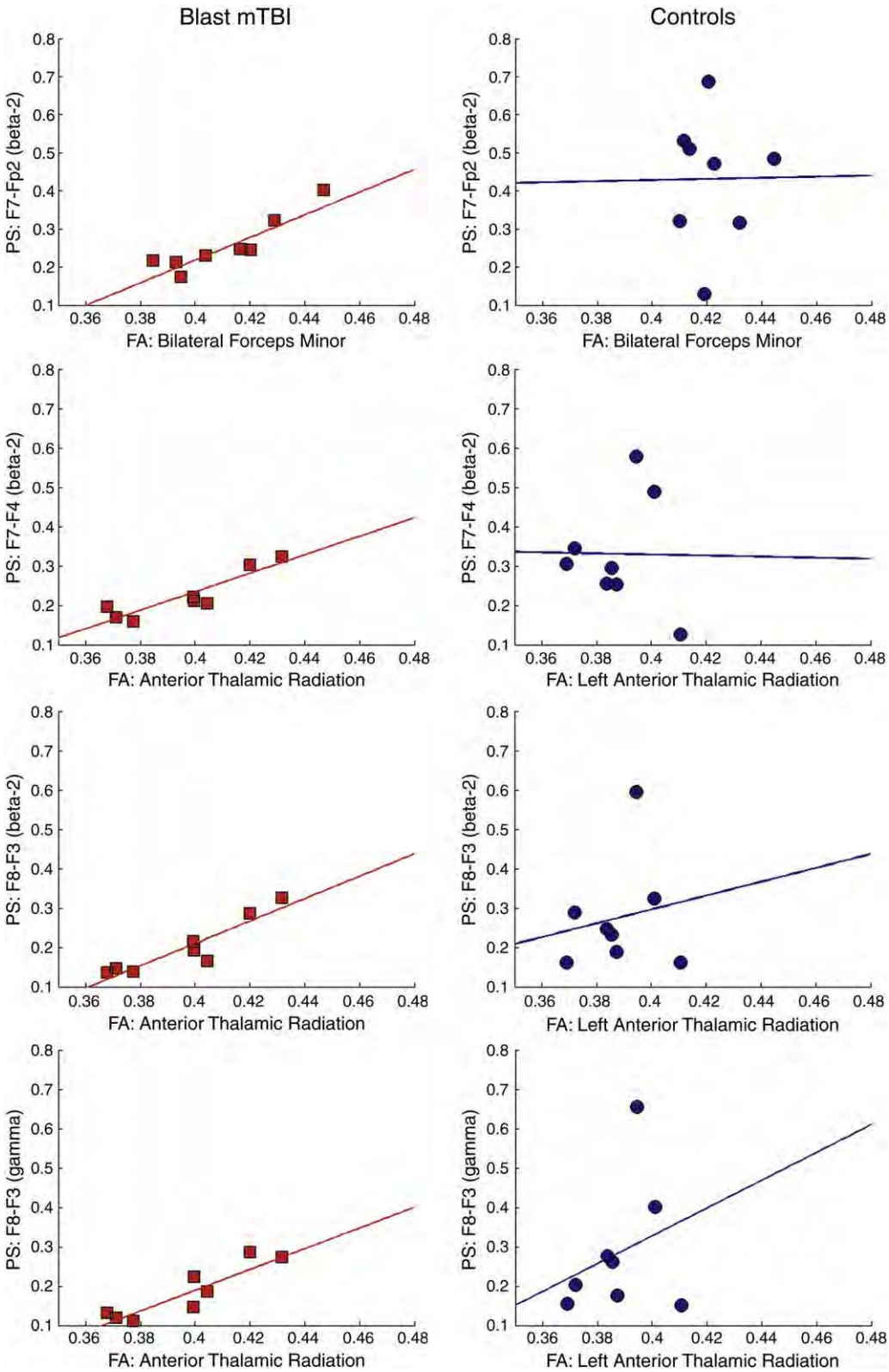

Fig. 4. Fractional anisotropy (FA) of the forceps minor and the left anterior thalamic radiations derived from diffusion tensor imaging (DTI) contrasted with the EEG phase synchrony (PS) between lateral frontal electrode sites (F7, F8) and opposite hemisphere frontal electrodes for beta and gamma frequency bands.

Absent from the findings was any indication of cognitive impairment in the blast-injured group. Studies suggest any cognitive impairment immediately after mTBI is brief and undetectable a month post injury. Because subjects had received only a mild TBI and it had occurred many months prior to study participation, an absence of cognitive impairment is expected. The mechanism by which cognitive functioning recovers after mTBI is unclear. Because the brain is an adaptive organ with dynamic interactions between neural structures it is reasonable to suppose that with damage the brain adopts an alternative neural pathway to complete a cognitive function. Thus, it is

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possible that in the studied sample there is an absence of functional impairment despite aberrant EEG phase synchrony than is associated with frontal white matter tract integrity.

Because this investigation focused on explosive blasts that injured soldiers in combat actions there are additional consequences to deployment and the blast events that can confound clear description of the effect of explosions on brain structure and function. Analyses testing possible confounds of diminished EEG phase synchronization in blast injured soldiers failed to yield evidence that factors other than blast mTBI explained the effect. EEG phase synchrony values were uncorrelated with self-reported PTSD and depression symptoms, and a formal diagnosis of PTSD was associated with greater phase synchrony for frequency bands and nonfrontal sites unrelated to phase synchrony effects associated with blast mTBI (see supplemental material). Thus, diminished phase synchrony in blast injured subjects could not be attributable to symptomatology indicative of mental disorders; however, the use of a behaviorally matched control group for PTSD and depression symptoms would better allow establishment of differences due to blast TBI. Prescription of antidepressants and sleep medications were associated with a tendency toward increased phase synchrony in different frequency bands at different electrode sites than the effect associated with blast injury, hence the findings appear unrelated to prescribed medication. Although clinical symptomatology and prescribed medications appeared not to be confounds, the present study is limited by a small sample size and control subjects that were not necessary military veterans and had not been deployed. Nevertheless, the blast injured and control groups were of comparable age, gender, IQ, and handedness and thus findings are unlikely to be the consequence of demographic influences.

The diminished EEG phase synchrony that was associated with the fractional anisotropy of frontal white matter tracts may be the functional expression of a pathological change in tissue. Because the association is most evident in the blast mTBI group, it suggests that structural alteration to the forceps minor and anterior thalamic radiation reduces the EEG phase synchrony of the regions innervated by these white matter tracts. If the association of phase synchrony with white matter tract integrity was evident in both groups then one could argue that the association has little to do with blast injury and instead reflects normative associations between white matter structure and brain function as reflected in the EEG. Also, evidence that the diminished phase synchrony is observed in a similar pattern for both hemispheres between frontal polar and opposite frontal lateral regions indicates that the effect is unlikely due to volume conduction or spurious recording characteristics. Though the presence of potential confounding factors and small sample size need to be taken into consideration, the results of the present study provide important initial evidence for measures of neural function being sensitive to the effects of blast injury despite normal cognitive functioning as assessed by an array of neuropsychological tests. If the present findings are replicated in larger and more definitive studies, serial complex EEG monitoring of combat veterans, together with DTI evaluations, may be necessary elements in the care of military personnel who have experienced non-impact, blast-related mTBI. The value of such testing would also depend on how functional and structural brain measures are associated with clinical variables, treatment response, and recovery.

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Conflict of interest statement

The authors do not have any actual or potential conflict of interest including financial or personal that could inappropriately influence, or be perceived to influence, their work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2010.09.007.

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Diffuse and spatially variable white matter disruptions are associated with blast-related mild traumatic brain injury

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Abstract

Mild traumatic brain injury (mTBI) due to explosive blast is common among military service members and often associated with long term psychological and cognitive disruptions. Little is known about the neurological effects of blast-related mTBI and whether they differ from those of impact (i.e. non-blast) mTBI. Given that brain damage from blasts may be diffuse and heterogeneous, we tested the hypothesis that blast mTBI is associated with subtle white matter disruptions in the brain that are spatially inconsistent across individuals. We examined a group of American military service members with (n=25) or without (n=33) blast-related mTBI who had been deployed as part of Operation Iraqi Freedom or Operation Enduring Freedom. History of impact mTBI was equally common across groups, which enabled testing of both blast and non-blast mTBI effects on white matter integrity as measured by fractional anisotropy (FA) derived from diffusion tensor imaging data. Two-way ANOVAs were used to test the effects of blast and past impact mTBI on measures sensitive to (1) concentrated, spatially consistent (average FA within a region of interest [ROI]), (2) concentrated, spatially variable (number of ROIs with abnormal average FA), and (3) diffuse (number of voxels with abnormal FA) disruptions of white matter integrity. Blast, but not impact, mTBI was associated with a diffuse, global pattern of lower white matter integrity. Neither type of mTBI had an effect on the measures sensitive to more concentrated and spatially consistent white matter disruptions. Additionally, individuals with more than one blast mTBI tended to have a larger number of aberrantly low FA voxels than individuals with a single blast injury. These results indicate that blast mTBI is associated with disrupted integrity of several white matter tracts, and that these disruptions are diluted by

averaging across the large number of voxels within an ROI. The reported pattern of effects supports the conclusion that the neurological effects of blast mTBI are diffuse, widespread, and spatially variable.
Keywords: traumatic brain injury, white matter, diffusion tensor imaging, blast

Abbreviations: TBI, traumatic brain injury; mTBI, mild traumatic brain injury; LOC, loss of consciousness; PTA, post-traumatic amnesia; PTSD, post-traumatic stress disorder.

1. Introduction

One of the most common injuries to military service members in recent conflicts is mild traumatic brain injury (mTBI) from explosive blast (Taber, D. L. Warden, & Hurley, 2006; D. Warden, 2006). Approximately 15-25% of American service members deployed to Iraq or Afghanistan reported mTBI (i.e. concussion), and explosive blast was involved in approximately 75% of these incidents (Hoge et al., 2008; Terrio et al., 2009; Wilk et al., 2010). The brain damage associated with mTBI has traditionally been believed to be minimal and temporary, supported by the relatively rapid reduction of symptoms and lack of gross abnormalities on structural neuroimaging scans like computed tomography (CT) and magnetic resonance imaging (MRI) (Niogi & Mukherjee, 2010). However, evidence of white matter disruptions in moderate and severe forms of TBI (Kasahara et al., 2010; Kinnunen et al., 2010; Levin et al., 2008; Oni et al., 2010; A. Sidaros et al., 2008), along with reports of persistent post-concussive symptoms in up to 30% of cases (Schneiderman, Braver, & H. K. Kang, 2008), raises the possibility of long-term neurological effects that may not be evident using traditional clinical and neuropsychological instruments.

Diffusion tensor imaging (DTI), an MRI technique used to assess microstructural properties of white matter, has generally demonstrated lower integrity of white matter tracts in frontal and temporal regions in individuals with mTBI relative to a healthy control group (for full review, see Niogi & Mukherjee, 2010). However, given that the directions of forces involved in the initial injury differ across cases (e.g. the orientation of the head relative to the impact), so too may the locations of injury within the brain. Consistent with multiple and varied areas of white matter being affected in mTBI, two studies have shown that the number of regions with "abnormally" low white matter integrity (i.e. fractional anisotropy [FA] several standard deviations below a control group mean) correlated with measures of trauma severity and cognitive function (Levin et al., 2008; Ptak et al., 2003). Because the specific regions with compromised white matter integrity varied across individuals in these studies it may be the number of areas with affected white matter, rather than the magnitude of damage within any single region, that is the most relevant aspect of the brain damage associated with mTBI (Ptak et al., 2003). Additionally, studies with data at multiple time points have failed to find an effect of time since injury on FA, suggesting that long-term neurological effects of mTBI may be present shortly after the injury (Inglese et al., 2005; Rutgers et al., 2008).

Blast and non-blast mTBI are qualitatively different in their origins and may carry different consequences for the structural and functional connectivity of the brain. For instance, most non-blast mTBI is due to impact injuries, such as automobile and sports-related collisions,

that involve acceleration-deceleration forces, whereas explosive blast involves a series of pressure waves with compressive and tensile components (Moore & Jaffee, 2010; Taber, D. L. Warden, & Hurley, 2006). The only published comparison of FA between individuals with blast mTBI and healthy controls failed to find effects in any region of interest (ROI) or using voxelwise comparisons (Levin et al., 2010). However, our previous work demonstrated that FA in soldiers who experienced blast mTBI correlated with electroencephalography (EEG) measures of functional connectivity between brain regions (Sponheim et al., 2010). Therefore, it is likely that neurological effects of blast injury are present, though their characterization may require different techniques than those used in impact mTBI.

In the current study, we examined military service members deployed to Operation Enduring Freedom or Operation Iraqi Freedom for effects of exposure to explosive blasts on the white matter of the brain. We hypothesized that the nature of blast creates a diffuse and widespread pattern of damage to which methods that average measures of white matter integrity within a region or across individuals are insensitive but that can be captured through the use of voxelwise z-scores that do not have strict spatial constraints. Thus, we predicted that blast mTBI would be associated with a greater number of abnormally low FA voxels (i.e. more points of compromised white matter integrity) but would not affect average FA within individual regions of interest.

2. Materials and Methods

2.1 Participants

Participants consisted of 25 veterans of Operation Enduring Freedom and Operation Iraqi Freedom who had been exposed during deployment to an explosive blast followed shortly thereafter by symptoms indicative of mTBI, and 33 veterans who had not experienced an explosive blast or any symptoms of blast-related mTBI. Subjects were recruited from an existing sample of National Guard soldiers, Minneapolis Veterans Affairs Medical Center patient rosters, and by word of mouth from other participants or service providers.

Symptoms of mTBI were assessed by self-report and included altered consciousness (e.g. confusion, disorientation), loss of consciousness (LOC) less than 30 minutes, post-traumatic amnesia (PTA) up to 24 hours, and neurological symptoms (e.g. headache, tinnitus, nausea, sensitivity to light or noise) immediately after the event. Blast injuries occurred 2-5 years prior to involvement in the study. Table 1 summarizes demographic and clinical characteristics of the groups.

2.2 Clinical Assessment

All participants underwent a clinical interview that included the Structured Clinical Interview for DSM-IV-TR (SCID; First, Spitzer, Gibbon, & Williams, 2002), Clinician-Administered Post-Traumatic Stress Disorder (PTSD) Scale (CAPS; Blake et al., 1995), and the Minnesota Blast Exposure Screening Tool (MN-BEST; Nelson et al., in press), a TBI rating scale developed for the project. Exclusionary criteria included diagnosis of current PTSD according to the CAPS so that any potential confound of combat stress conditions would be limited, as well as native language other than English, current or pre-deployment unstable medical condition that would affect brain function (e.g. anoxic episode greater than 10 seconds, stroke, seizures, multiple sclerosis, etc.), uncorrected visual or auditory disturbances, moderate or severe TBI not due to blast, any pre-deployment DSM-IV Axis I condition requiring treatment, and contraindications to MRI (e.g. metallic implants, shrapnel, claustrophobia).

As a measure of re-experiencing of traumatic events (including explosive blasts), each of the five Criterion B symptoms for PTSD was assessed using the CAPS by summing 5 point scales (0-4) of intensity and frequency for total possible CAPS B scores ranging between 0-40. Using the MN-BEST we assessed the 3 most significant blast-related and impact-related head injuries, each of which received a severity score ranging from 0 (no concussion) to a potential maximum of 30 (severe TBI), though no score was higher than 4 (LOC 5-30 minutes or PTA >12 hours) in the current sample. Blast-related injuries were defined as those in which the individual felt a blast wave and attributed the resultant concussion to its effects, though secondary and tertiary effects, such as being thrown against the ground or being hit by a projectile, were acceptable. Impact injuries, including civilian injuries (e.g., high school sports concussions) and non-blast deployment injuries (e.g. falling off a wall or vehicle), were assessed on the same scale. TBI ratings were completed by doctoral-level neuropsychologists based on descriptions of events secured by study interviewers. DSM diagnoses, including PTSD, were finalized by advanced doctoral students whose work was supervised and reviewed by doctoral-level licensed psychologists.

Participants completed an informed consent process that included complete description of the study, and participants were provided with monetary compensation for their participation after each study procedure. The study was approved by the University of Minnesota and Minneapolis Veterans Affairs Medical Center Institutional Review Boards.

2.3 Image Acquisition and Processing

Images were acquired on a 3 Tesla Siemens Trio (Erlagen, Germany) scanner using a 12-channel birdcage head coil. Head movements were minimized by placing pads around the participant's head. Localizers were acquired for orientation and prescription of subsequent scans. A high resolution MP-RAGE structural image (repetition time [TR]=2,530 ms, echo time [TE]=3.65 ms, 240 coronal slices, 256x256 matrix, 256mm field of view [FOV], 1.0mm thickness) was collected for anatomical alignment and visualization. Two sets of diffusion weighted images aligned to the plane including the anterior and posterior commissures were collected in each of 30 noncollinear directions at b=800 s/mm^2, along with 10 images collected with no diffusion weighting evenly distributed throughout the sequence. Other parameters included TR/TE=9000/84 ms, 72 oblique axial slices, 128x128 matrix, 256mm FOV, 2.0 mm thickness. A field map of the DTI space was collected immediately following the DTI sequence.

We used the FMRIB software library (FSL; Smith et al., 2004; Woolrich et al., 2009) tools to co-register the diffusion-weighted images to remove small movements that may have occurred during the sequence, remove eddy currents, and correct field inhomogeneity artifacts using the field map. Fractional anisotropy (FA) values were computed at each brain voxel (Basser, Mattiello, & LeBihan, 1994; Basser & Pierpaoli, 1996).

2.4 Statistical Analyses

2.4.1 Demographic and clinical characteristics

Gender and the presence of impact mTBI were compared across groups using chi-squared statistics. Age was compared across groups with a t test, and total scores on the Criterion B items of the CAPS (i.e. total CAPS B scores) and on the impact TBI scale were compared across groups with Mann-Whitney U tests to account for the non-normal distribution.

2.4.2 Average FA within regions of interest (ROI)

To determine whether the FA of specific tracts was affected by mTBI, a set of 20 standard probabilistic tractography-based ROIs (Mori, Wakana, Zijl, & Nagae-Poetscher, 2005) was thresholded at 25% probability in standard space, as shown in Figure 1, and registered to each subject's DTI space using nonlinear transformations (FNIRT; Andersson, Jenkinson, & Smith, 2007a; Andersson, Jenkinson, & Smith, 2007b). These ROIs were selected because they encompass the major subcortical white matter tracts. For each ROI, FA was averaged across all voxels in which FA > .20 to ensure that only white matter voxels were included. Since impact mTBI was common in both groups of service members, average FA was compared among groups with a 2-way analysis of variance (ANOVA) with blast mTBI and impact mTBI as

the two factors so that the effects of each could be tested. Each main effect was corrected for multiple comparisons separately using a false discovery rate of q=0.05 (Genovese, Lazar, & Nichols, 2002).

2.4.3 Number of regions with aberrantly low average FA

Given the heterogeneous nature of blast-related head injury, it is possible that a different set of white matter tracts is affected in each individual. In this case, each ROI would only be affected in a subset of individuals, which would reduce the likelihood of detecting an effect in any single ROI. To determine whether the specific tracts affected by mTBI varied across individuals, we compared the number of ROIs with abnormally low average FA without requiring the same regions to be abnormal across subjects. The mean and standard deviation of the average FA measures in each ROI were computed across the 14 non-TBI participants (i.e. participants who had neither blast nor impact mTBI), and each participant's average FA scores were converted to z-scores by subtracting the mean and dividing by the standard deviation of the respective ROIs. For each individual we then determined the number of ROIs out of 20 with FA more than 2.0 standard deviations below the "healthy" mean (i.e. $z < -2.0$). The tallies of ROIs with aberrantly low FA were converted to ranks to account for their non-normal distribution and compared using a 2-way ANOVA as described above.

2.4.4 Number of voxels with aberrantly low FA

Both preceding methods assume that mTBI affects entire tracts, or at least affects substantial enough portions of tracts to create a detectable effect on the average. To determine whether small regions, rather than entire tracts, were affected by mTBI, we compared the number of voxels with abnormally low FA with minimal spatial constraints across subjects. Each subject's FA map was registered to standard space by inverting the nonlinear transformation computed in 2.4.2 to align the ROIs to native space. Images of the mean and standard deviation at each voxel were created based on the 14 non-TBI participants (see Supplemental Figure 1) and used to create z-score maps for each subject, which were then thresholded at -2.0. A mask was created to restrict further processing to those voxels in which FA was greater than 0.20 in all subjects. The number of aberrant (i.e. $z < -2.0$) voxels within each ROI was counted, rank-transformed, and compared using the 2-way ANOVA described above. The total number of aberrant voxels *across all 20 ROIs* and the total number of aberrant voxels *across the entire white matter mask* (which subsumed the 20 ROIs as well as non-ROI white matter regions) were also counted, rank-transformed, and compared in the same manner. Significant

main effects were followed up with Mann-Whitney U tests to better characterize group differences.

3. Results

3.1 Demographic and clinical characteristics

As seen in Table 1, groups did not differ on gender composition, age, percentage of participants with impact mTBI, or impact head injury scores (all $p>0.05$). Table 2 presents the distribution of blast and impact mTBI within the sample. Individuals with blast mTBI had somewhat higher scores on the Criterion B items of the CAPS than those without blast mTBI ($t=2.40$, $p=0.02$), indicating higher re-experiencing of trauma, though none of the subjects met diagnostic criteria for PTSD. This difference is expected given that the blast exposure constituted a traumatic experience for many individuals.

3.2 Number of voxels with aberrantly low FA

Blast mTBI was associated with a greater number of voxels with low FA (i.e. low white matter integrity) in 14 of the 20 ROIs after correcting for multiple comparisons. Regions demonstrating this effect included the forceps major and minor, bilateral anterior thalamic radiations, bilateral cingulum, right corticospinal tract, bilateral inferior frontal occipital fasciculus (IFOF), bilateral inferior longitudinal fasciculus (ILF), bilateral superior longitudinal fasciculus (SLF), and right temporal portion of the SLF. Table 3 summarizes these effects, and Figures 2 and 3 demonstrate properties of the underlying histograms. Blast mTBI was also associated with a greater number of low FA voxels across all ROIs and across the entire white matter mask (both $F_{1,54} > 16.0$, $p<0.001$), indicating that blast injury was associated with a greater frequency of voxels with low white matter integrity, although the particular locations within and across ROIs varied across individuals. Supplemental Figure 4 demonstrates the distribution of aberrant voxels in two representative participants. According to the follow-up Mann-Whitney U group comparison of blast mTBI, ten regions and the two summary measures that included a majority of white matter in the brain demonstrated significant effects that survived correction for multiple comparisons, as shown in Table 3.

Impact mTBI was not significantly associated with any difference in the number of voxels with low FA in any individual region, though it was associated with a greater number of low FA voxels across all ROIs ($F_{1,54}=5.33$, $p=.025$) and across the entire white matter mask ($F_{1,54}=5.87$, $p=.019$).

3.3 Average FA within regions of interest and number of regions with aberrantly low average FA

When FA was averaged across voxels within an ROI, rather than tallying the number of aberrantly low FA voxels, no ROIs revealed an effect of blast or impact mTBI. Likewise, the number of ROIs with aberrantly low average FA failed to differ among groups. Thus, averaging FA across multiple voxels within an ROI did not reveal any white matter abnormalities associated with either form of mTBI.

3.4 Effect of multiple blast mTBIs

Based on the observation that a subset (n=7) of the blast mTBI group had experienced more than one blast mTBI event, we conducted an unplanned follow-up analysis to determine whether additional blast mTBI events were associated with a greater degree of white matter integrity disruption. Specifically, we used a one-way ANOVA to compare the total number of low FA voxels across the entire white matter mask among the three groups, defined as no blast (n=33), single blast (n=18), and multiple blasts (n=7). As expected, the effect of group was highly significant ($F_{2,55}$=10.04, p<.001), and Tukey post hoc statistics indicated that both blast groups had higher mean rank (i.e. larger number of low FA voxels) than the no blast group (p<.01). In addition, the group with multiple blast mTBI events tended to have higher mean ranks than the single blast group (Figure 4), though this difference did not reach significance according to Tukey post hoc statistics (p>.20).

4. Discussion

We used a combination of analysis strategies to assess the long-term effects of blast and impact mTBI on white matter integrity in a sample of American military service members. Blast mTBI was associated with a greater number of voxels with abnormally low FA in a majority of a priori defined brain regions and in total white matter, while traditional ROI methods failed to reveal effects of either type of injury. Furthermore, the number of low FA voxels was especially high in individuals with multiple blast mTBI events. This suggests that the long-term effects of blast mTBI on white matter integrity consist of subtle, widespread disruptions rather than damage to specific tracts that is consistent across individuals. Impact mTBI was not associated with reduced white matter integrity using any of the 3 techniques, suggesting that the effect of impact mTBI on FA appears to be minimal in this population. Evidence of FA abnormalities years after the injury is important given the controversy over how persistent post-concussive symptoms should be interpreted and treated in a military setting (Vasterling, Verfaellie, & Sullivan, 2009). To date, the overlap of mTBI and PTSD symptomatology has made it difficult to

determine the relative contributions of each condition to the impairments of returning service members and to determine the appropriate treatment. The current results indicate that blast mTBI is indeed associated with long-term white matter disruption, perhaps uniquely as compared to PTSD (Sponheim et al., 2010). Further research is required to determine how to best use this information on an individual case basis.

The use of a military control population in the present study helped to control for the potential physical and psychological effects of deployment, as well as personality characteristics and other features common among members of the military. Thus, the design substantially reduces extraneous differences between groups. Additionally, the similar distribution of impact mTBI between the groups with and without blast mTBI is helpful in separately assessing the effects of each. The substantial representation of impact mTBI across groups indicates the need to consider prior impact injuries when assessing the effects of blast mTBI in military populations.

The observation of effects for blast, but not impact, mTBI has several interpretations. It is possible that the context and mechanism of blast-related head injury produces greater white matter disruption than non-blast injuries. For example, the architecture of the skull and meninges may be better suited to absorb the impact of acceleration-deceleration forces that are common in nature than those of pressure waves that are rare. It is also possible that the context of deployment, including disrupted sleep, dehydration and exhaustion, and a heightened state of physiological arousal, prevented the brain from healing as fully afterwards. The most straightforward explanation for the discrepancy, however, may be that the blast injuries were more homogeneous than the impact injuries in terms of timing (e.g. during early adulthood, 2-5 years before imaging), context (i.e. deployment), and nature (i.e. pressure wave originating at a distance on the order of tens of meters) as compared to impact injuries that could have occurred during childhood and involved a variety of origins. The failure to find any effect of impact mTBI on FA is somewhat inconsistent with previous reports in civilian populations that document reduced FA in a range of brain areas, which could reflect differences between military and civilian populations unrelated to deployment, or military deployment may itself have effects on the brain that simply add variance and thus make detection of impact mTBI effects more difficult.

4.1 Limitations

One difficulty of using z-scores as a dependent variable is that the results are only as reliable as the estimates of means and standard deviations on which they are based. In

particular, poor estimation of the mean within the control group can lead to an artificial overabundance of extreme values in the other groups. In the current study, z-scores were based on the 14 subjects with no history of mTBI, so it is possible that the number of aberrant voxels in the affected groups was somewhat inflated by this bias. However, to include subjects who are hypothesized to have "abnormal" FA in at least a subset of voxels in the estimation of the distribution would introduce its own bias. In an attempt to address this, we conducted a supplemental analysis (see Supplemental Figures 3-5) that included each voxel's immediate neighbors in the estimation of its mean and standard deviation and thus used seven times the data. This process provided more stable estimates of the mean by reducing Gaussian measurement error at the expense of an increased standard deviation due to spatial heterogeneity. The results using this method were similar to those of the primary study in that blast mTBI was associated with a greater number of low FA voxels in 11 regions and overall (see Supplemental Table) and that impact mTBI had an effect only in the left anterior thalamic radiations and when all voxels were considered. Although this provides evidence that the results are not an artifact of poor distribution estimation, a larger healthy population would be the optimal method of addressing this concern.

5. Conclusions

Our analyses demonstrated widespread white matter disruptions associated with blast-related mTBI to which standard ROI methods were insensitive. In contrast, a history of impact (i.e., non-blast) mTBI failed to be associated with white matter disruption, perhaps indicating a difference in the mechanism of action between the types of mTBI. It will be important in the future to obtain longitudinal data and to explore the functional consequences of blast-induced white matter disruptions.

Acknowledgements

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Table 1. Demographic and clinical characteristics of the sample.

	Blast	No Blast	Statistical tests
N	25	33	
Percent female	4%	15%	*ns*
Percent with impact mTBI	56%	58%	*ns*
Age in years: mean (SD)	36.0 (8.9)	32.5 (8.6)	*ns*
Range	24-55	22-52	
CAPS B total (median)	5	0	z=-2.61, p=.009
Range	0-18	0-17	
Blast TBI Index (median)	2		
Range	1-6		
Impact TBI Index (median)	2	2	*ns*
Range	0-9	0-7	

TBI=traumatic brain injury, mTBI=mild TBI, CAPS B total = total of severity and frequency ratings of PTSD Criterion B symptoms from the CAPS. Blast and Impact TBI Indexes represent summed severity scores of the 3 most significant injuries of each type.
ns = not significant

Table 2. Composition of groups.

		Impact		
		Yes	No	
Blast	Yes	Both (n=14)	Blast Only (n=11)	Blast (n=25)
	No	Impact Only (n=19)	No TBI (n=14)	No Blast (n=33)
		Impact (n=33)	No Impact (n=25)	Total (n=58)

Table 3: Percentage of abnormally low FA voxels, compared between participants with and without blast mTBI.

Region of interest	No Blast % median (range)	Blast % median (range)	z	p
Interhemispheric tracts				
Forceps major	1.21 (0.2-26.4)	4.08 (0.5-21.8)	**-3.52***	<.001
Forceps minor	1.21 (0.1-10.0)	2.80 (0.4-10.2)	**-2.60***	.009
Subcortical-cortical tracts				
Left anterior thalamic radiations	1.44 (0.2-5.3)	2.84 (0.4-13.7)	**-2.87***	.004
Right anterior thalamic radiations	1.26 (0.1-6.7)	2.59 (0.3-11.5)	**-3.17***	.002
Left corticospinal tract	2.09 (0.0-10.6)	2.98 (0.0-15.5)	-1.18	.239
Right corticospinal tract	1.73 (0.0-10.2)	3.54 (0.3-14.1)	**-3.04***	.002
Temporal lobe tracts				
Left IFOF	1.03 (0.1-6.7)	2.82 (0.4-8.4)	**-3.57***	<.001
Right IFOF	0.83 (0.1-5.9)	2.19 (0.1-11.0)	**-2.86***	.004
Left ILF	1.39 (0.0-6.3)	2.98 (0.5-12.3)	**-3.31***	.001
Right ILF	1.24 (0.0-8.3)	3.27 (0.1-10.5)	**-2.44***	.015
Left temporal SLF	0.00 (0.0-17.6)	2.94 (0.0-23.5)	-1.77	.076
Right temporal SLF	0.68 (0.0-38.6)	2.03 (0.0-18.0)	-2.18*	.029
Left uncinate	0.98 (0.0-12.5)	1.71 (0.0-28.9)	-1.19	.235
Right uncinate	0.63 (0.0-19.2)	1.05 (0.0-11.2)	-1.10	.270
Left cingulum/hippocampus	0.26 (0.0-5.9)	0.26 (0.0-5.2)	-0.86	.389
Right cingulum/hippocampus	0.40 (0.0-4.6)	1.00 (0.0-10.4)	-1.81	.070
Fronto-parietal tracts				
Left cingulum	1.66 (0.1-29.4)	3.98 (0.0-15.8)	-2.08*	.037
Right cingulum	1.88 (0.0-44.0)	3.50 (0.4-26.5)	-2.11*	.035
Left SLF	1.75 (0.1-10.8)	2.97 (0.2-8.1)	**-2.94***	.003
Right SLF	2.09 (0.1-15.6)	3.74 (0.3-13.5)	-2.01*	.044
Summary measures				
Total of ROIS	1.71 (0.5-7.4)	3.51 (0.6-8.8)	**-3.46***	.001
Total of white matter mask	1.69 (0.5-8.6)	3.40 (0.9-10.8)	**-3.70***	<.001

Voxel counts converted to percentages of total volume of each region of interest (ROI). Estimates of z and p are based on Mann-Whitney U comparison of ranks. Bold values represent regions in which participants with blast mTBI had significantly higher likelihood of abnormally low FA voxels than participants without blast mTBI, corrected for multiple comparisons (α=.05, FDR q=.05).

* Regions in which the main effect of blast TBI was significant in the 2-way ANOVA, corrected for multiple comparisons (α=.05, FDR q=.05).

Supplemental Table and Figures 3-5: An alternative method for computation of voxelwise z-scores was implemented in which neighboring voxels were included to provide more stable estimates of means and standard deviations.

Supplemental Table. Percentage of voxels with low FA, compared between participants with and without blast mTBI, when neighboring voxels are used in calculating z-scores.

Region of interest	No Blast % median (range)	Blast % median (range)	z	p
Interhemispheric tracts				
Forceps major	0.43 (0.0-14.4)	1.30 (0.0-13.8)	**-2.82**	.005
Forceps minor	0.25 (0.0-5.0)	1.10 (0.0-5.3)	**-2.60**	.009
Subcortical-cortical tracts				
Left anterior thalamic radiations	0.68 (0.0-4.1)	1.66 (0.3-9.1)	**-3.69**	<.001
Right anterior thalamic radiations	0.70 (0.0-4.9)	1.84 (0.0-8.5)	**-3.35**	.001
Left corticospinal tract	1.04 (0.0-8.1)	1.60 (0.0-12.3)	-1.06	.289
Right corticospinal tract	0.66 (0.0-9.1)	1.61 (0.0-10.1)	**-2.72**	.007
Temporal lobe tracts				
Left IFOF	0.21 (0.0-3.6)	1.45 (0.0-6.5)	**-3.46**	.001
Right IFOF	0.42 (0.0-3.5)	0.86 (0.0-8.6)	**-2.55**	.011
Left ILF	0.90 (0.0-4.8)	2.31 (0.0-10.6)	**-3.40**	.001
Right ILF	0.65 (0.0-4.6)	1.90 (0.5-7.6)	**-2.58**	.010
Left temporal SLF	0.00 (0.0-19.0)	3.17 (0.0-25.4)	-1.90	.057
Right temporal SLF	0.68 (0.0-37.8)	1.69 (0.0-15.5)	-2.05	.041
Left uncinate	0.27 (0.0-3.4)	0.27 (0.0-14.7)	-0.85	.394
Right uncinate	0.00 (0.0-7.7)	0.23 (0.0-2.1)	-1.93	.053
Left cingulum/hippocampus	0.00 (0.0-1.0)	0.00 (0.0-3.3)	-1.60	.111
Right cingulum/hippocampus	0.00 (0.0-1.2)	0.00 (0.0-4.0)	-1.77	.077
Fronto-parietal tracts				
Left cingulum	0.42 (0.0-15.7)	2.02 (0.0-11.4)	-**2.53**	.011
Right cingulum	0.15 (0.0-23.6)	0.88 (0.0-13.9)	-1.94	.052
Left SLF	0.82 (0.0-6.3)	2.36 (0.0-5.7)	**-3.60**	<.001
Right SLF	1.07 (0.0-10.4)	2.12 (0.2-7.7)	-1.80	.072
Summary measures				
Total of ROIS	0.86 (0.2-3.9)	2.07 (0.4-5.4)	**-3.76**	<.001
Total of white matter mask	0.90 (0.1-5.5)	2.24 (0.6-7.5)	**-3.92**	<.001

Voxel counts converted to percentages of total volume of each region of interest (ROI). Estimates of z and p are based on Mann-Whitney U comparison of ranks. Bold values represent regions in which participants with blast mTBI had significantly higher likelihood of abnormally low FA voxels than participants without blast mTBI, corrected for multiple comparisons (α=.05, FDR q=.05).

Figure Legends

Figure 1. Three-dimensional representation of the regions of interest (ROIs). Fmaj=forceps major, Fmin=forceps minor, ATR=anterior thalamic radiations, Cing/hip=hippocampal portion of cingulum, Cing=cingulum, CST=corticospinal tract, IFOF=inferior fronto-occipital fasciculus, ILF=inferior longitudinal fasciculus, SLF=superior longitudinal fasciculus, tSLF=temporal portion of SLF, Unc=Uncinate

Figure 2. Median cumulative distributions. Median cumulative distributions of abnormally low FA voxels in the (*top*) total white matter mask and (*bottom*) left inferior fronto-occipital fasciculus (IFOF). Three-dimensional representations of the masks are provided for reference.

Figure 3. Histograms of voxelwise z-scores. Histograms of voxelwise z-scores across all voxels within the white matter mask (*top*), the difference between group histograms (*middle*), and the differences from the histogram of the No TBI group (*bottom*).

Figure 4. Effect of number of blasts on total number of voxels with abnormally low FA. Rank-transformed counts of voxels across the entire white matter mask with abnormally low FA for individuals with no blasts (n=33), 1 blast (n=18), or more than 1 blast (n=7). Error bars indicate 95% confidence intervals.
** p<.01, difference from no blast group according to Tukey post hoc test

Supplemental Figure 1. Mean and standard deviation images. Figures demonstrating the mean (*left*) and standard deviation (*right*) of FA within the group with no history of TBI. These images were the basis of the calculation of voxelwise z-scores.

Supplemental Figure 2. Distribution of voxels with abnormally low FA. Voxels with FA more than 2 standard deviations below the mean in the median participant from the blast (*green*) and no blast (*red*) groups, overlaid on the mean FA image. Axial slices represent z=4.0mm (*blue*) and z=11.0mm (*yellow*) above the AC-PC plane in standard space.

Supplemental Figure 3. Mean and standard deviation images when neighboring voxels were included. Figures demonstrating the mean (*left*) and standard deviation (*right*) of FA within the group with no history of TBI when neighboring voxels were included. These images were the

basis of the calculation of voxelwise z-scores used in Supplemental Table and Supplemental Figures 4 and 5.

Supplemental Figure 4. Median cumulative distributions. Median cumulative distributions of abnormally low FA voxels in the (*top*) total white matter mask and (*bottom*) left inferior fronto-occipital fasciculus (IFOF).

Supplemental Figure 5. Histograms of voxelwise z-scores. Histograms of voxelwise z-scores across all voxels within the white matter mask (*top*), the difference between group histograms (*middle*), and the differences from the histogram of the No TBI group (*bottom*).

Figure 1 Color

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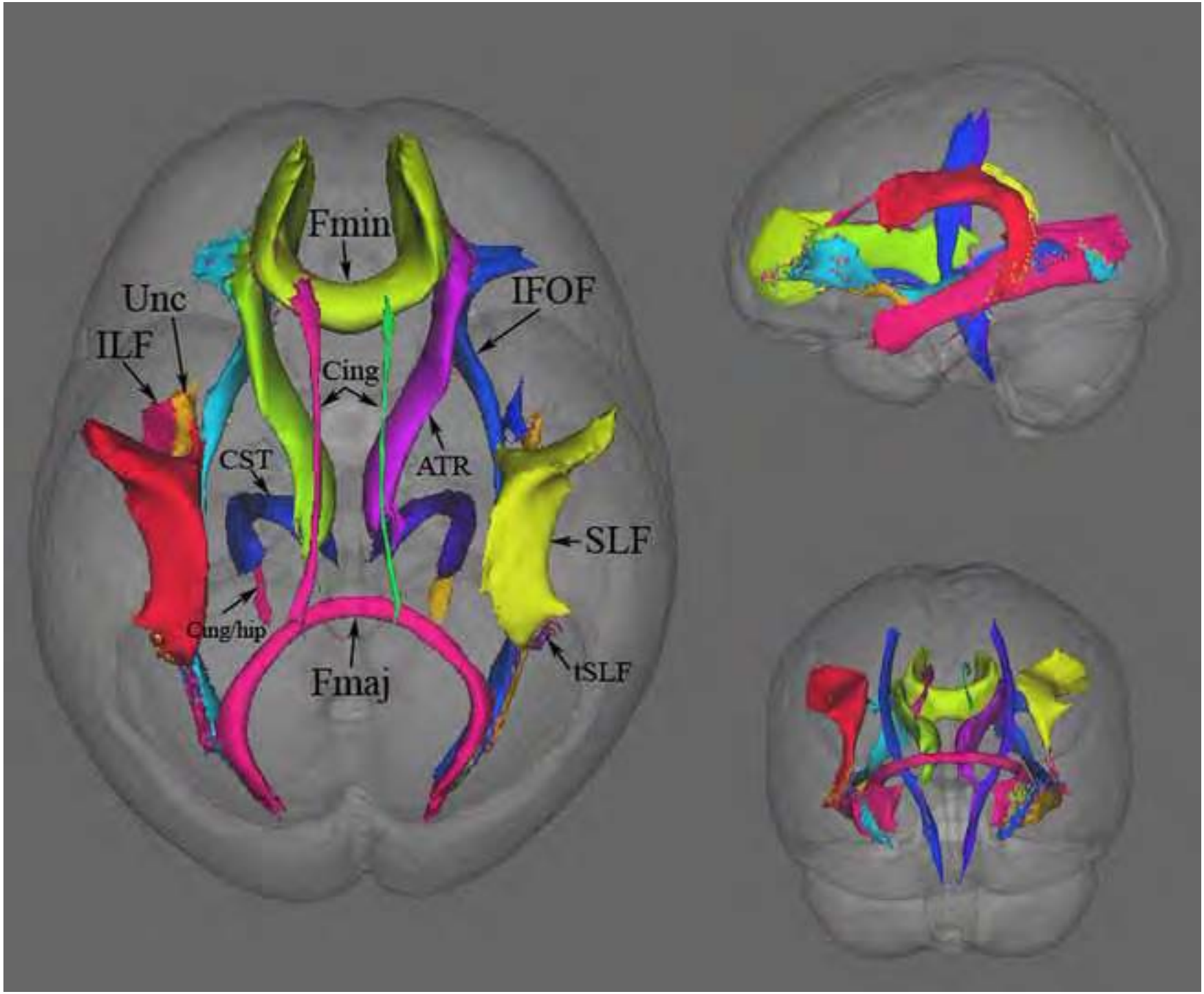

Figure 1 Grayscale

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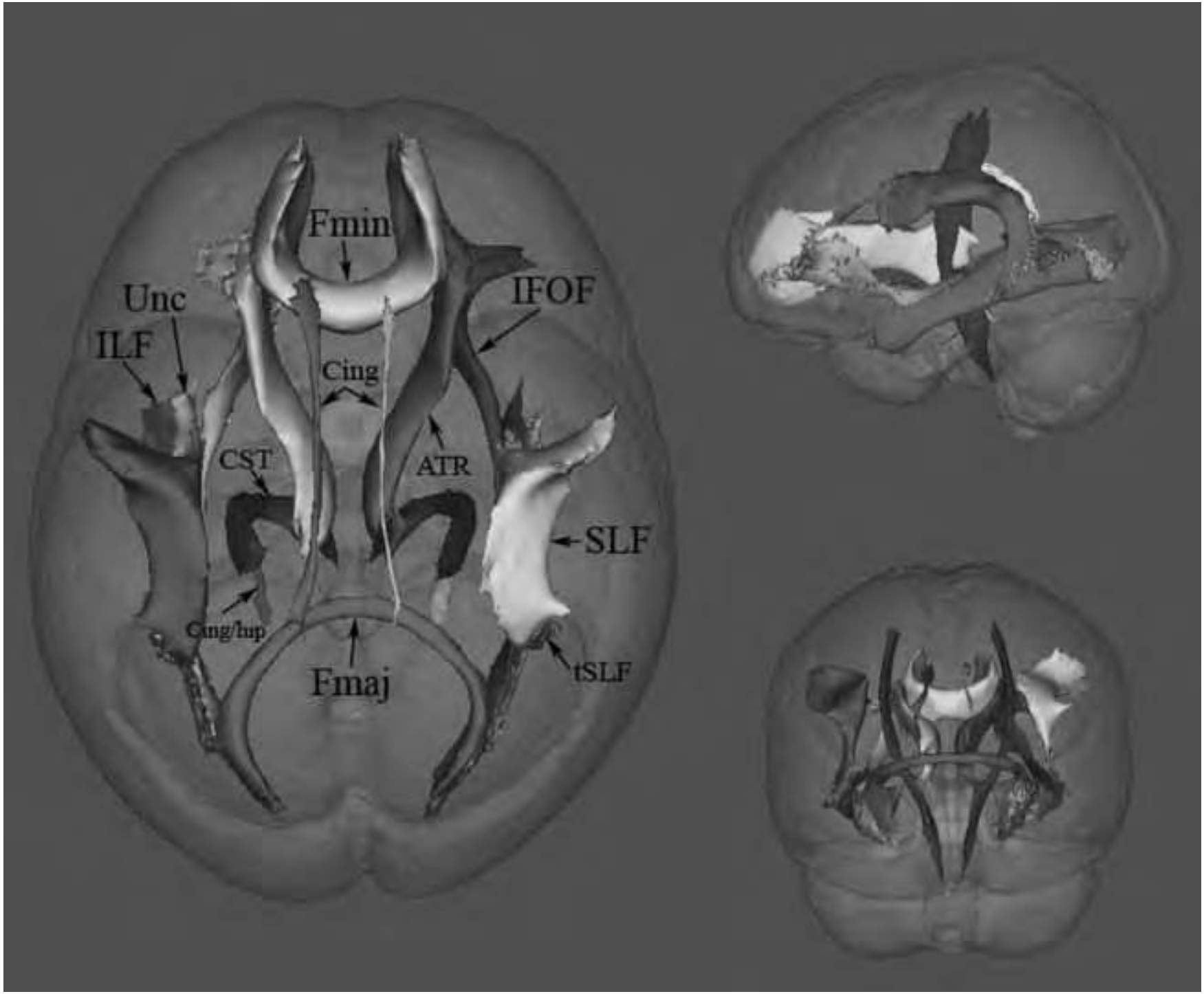

Figure 2 Color

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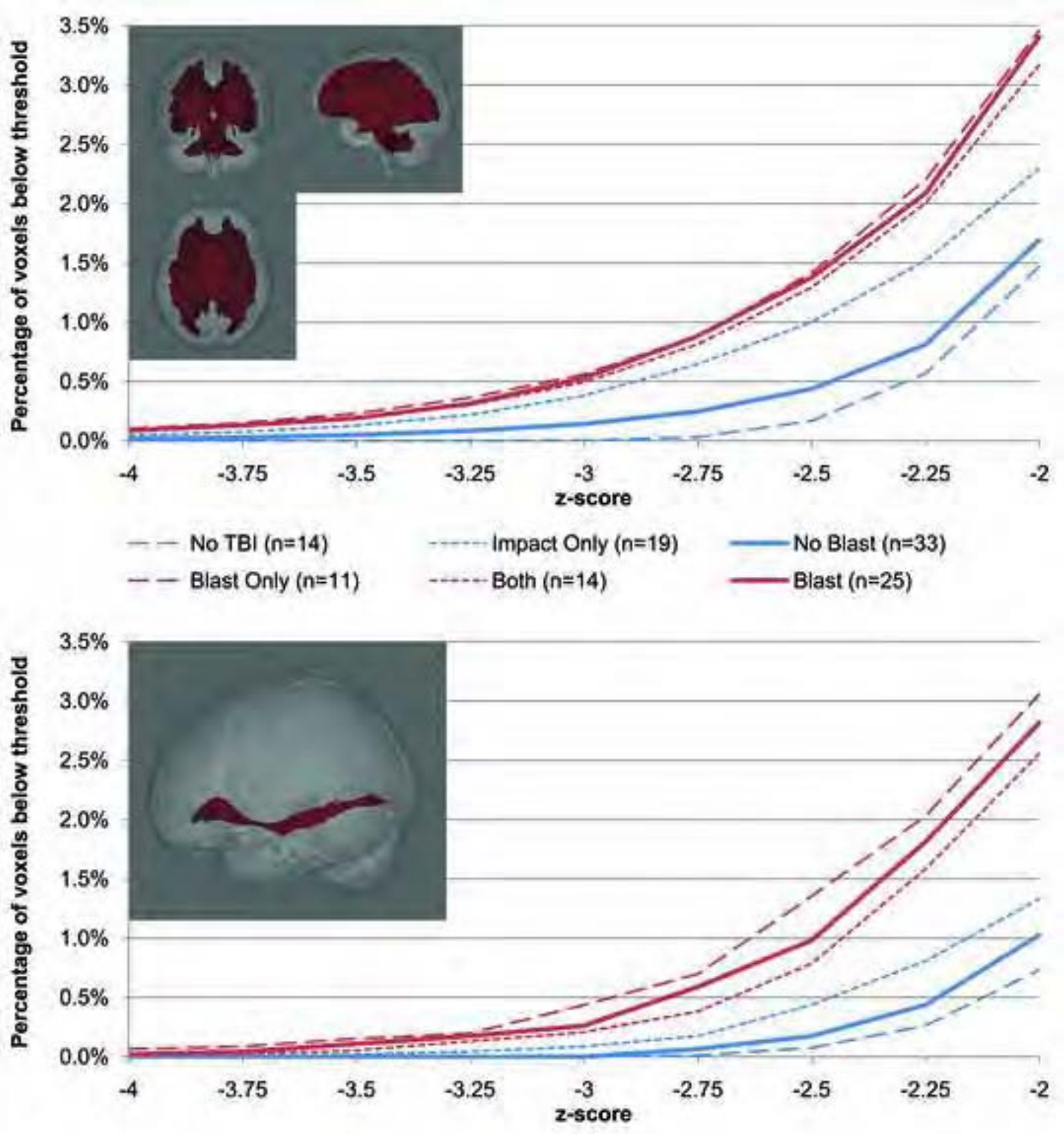

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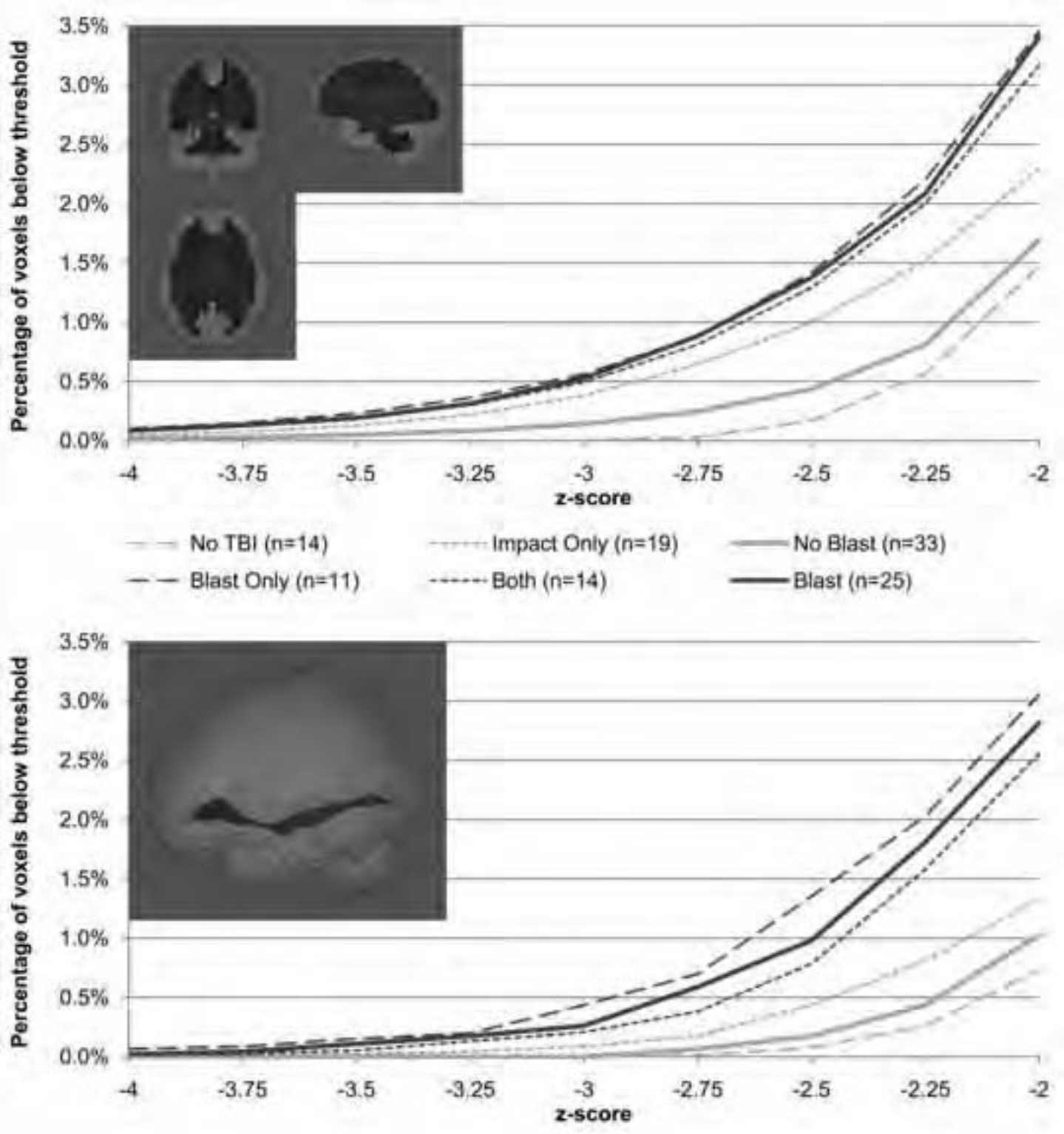

Figure 3 Color

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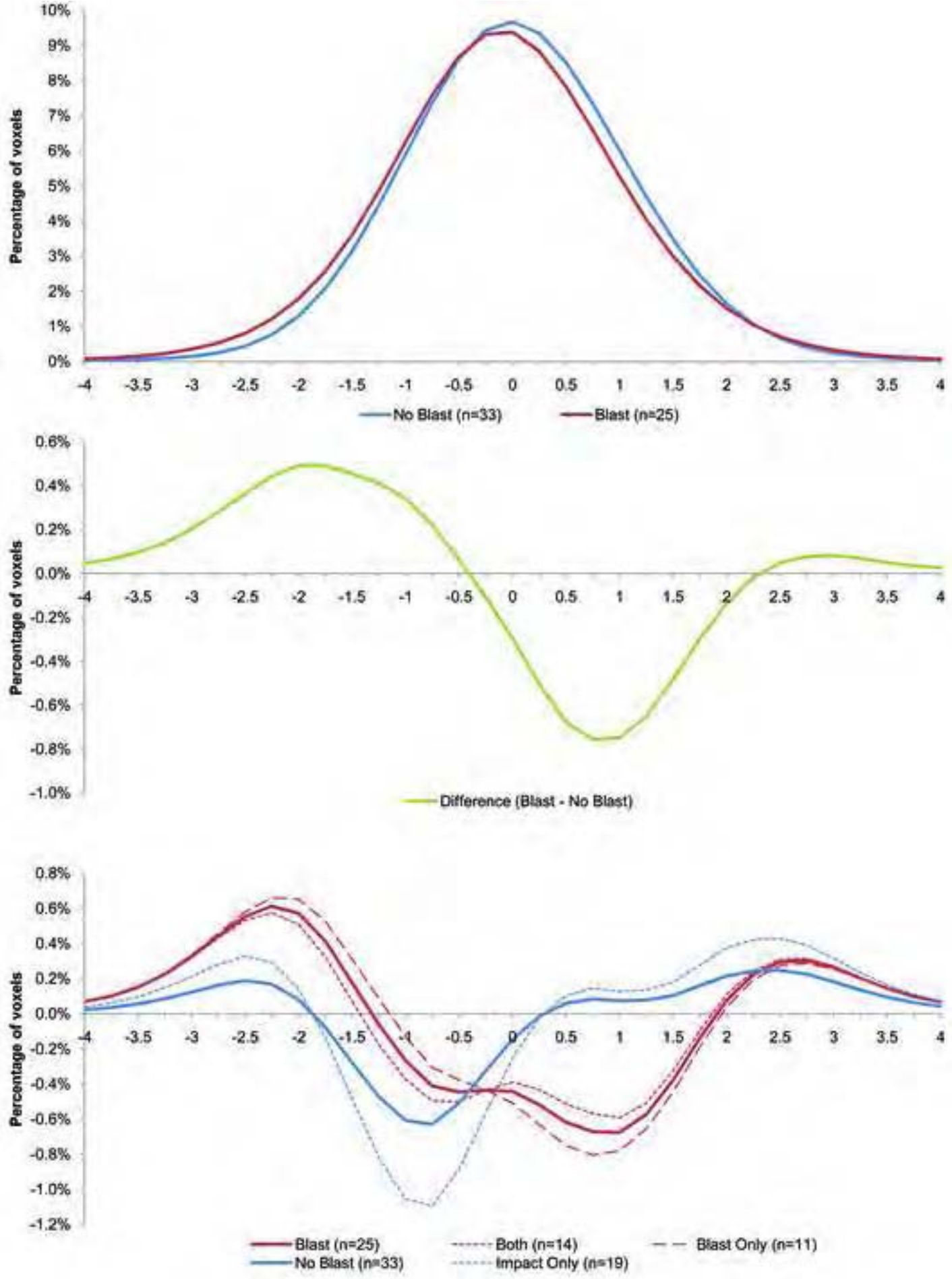

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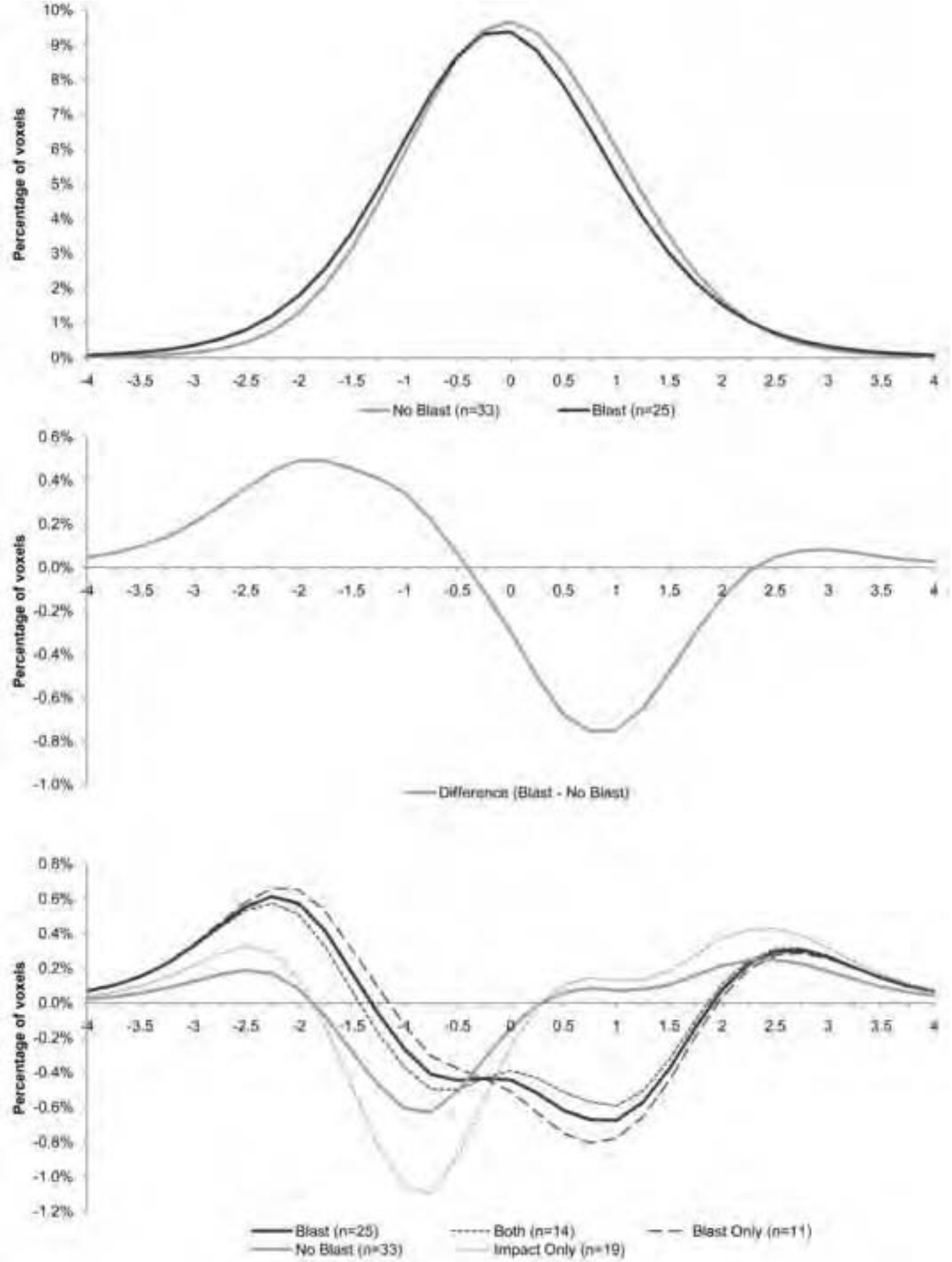

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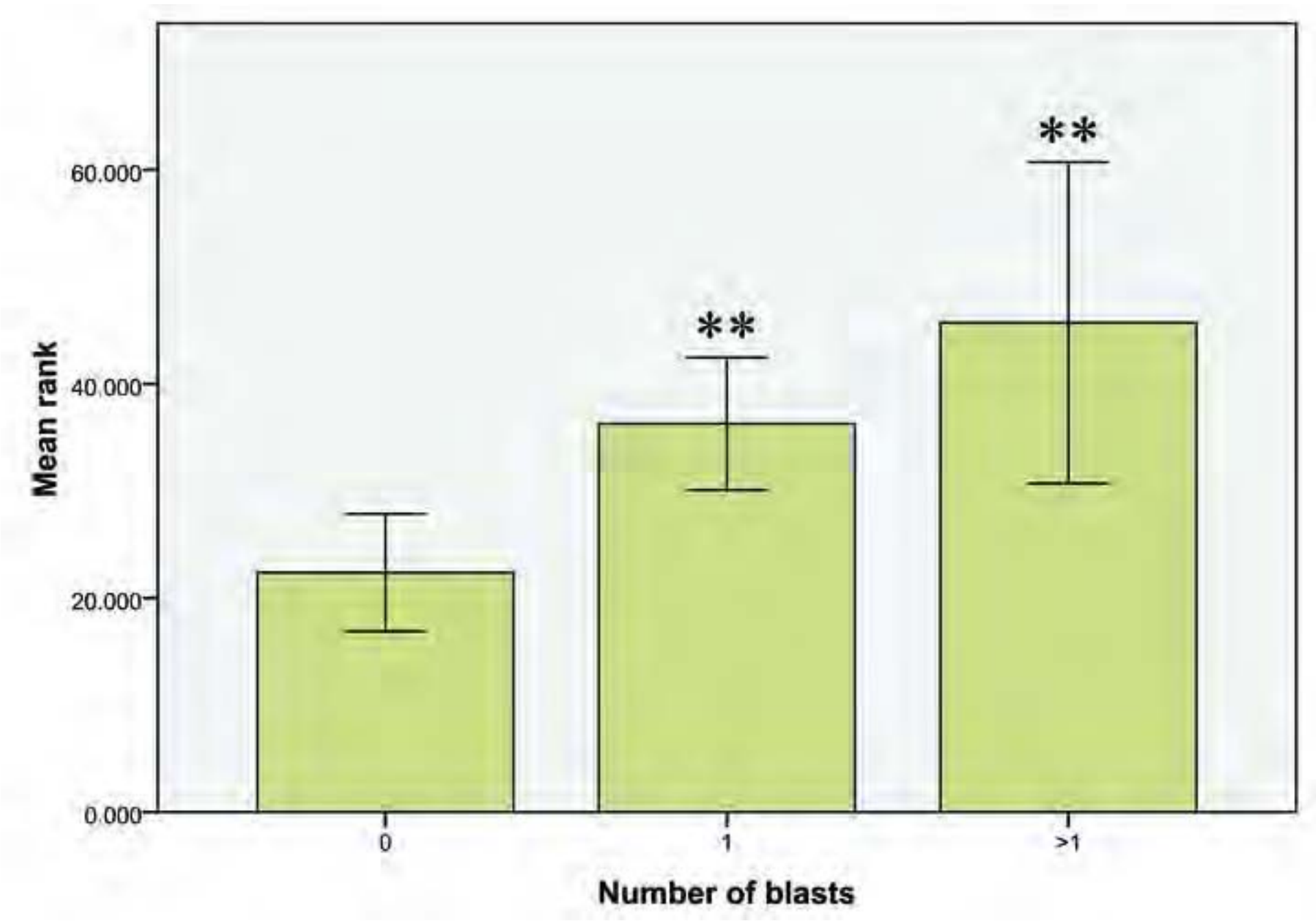

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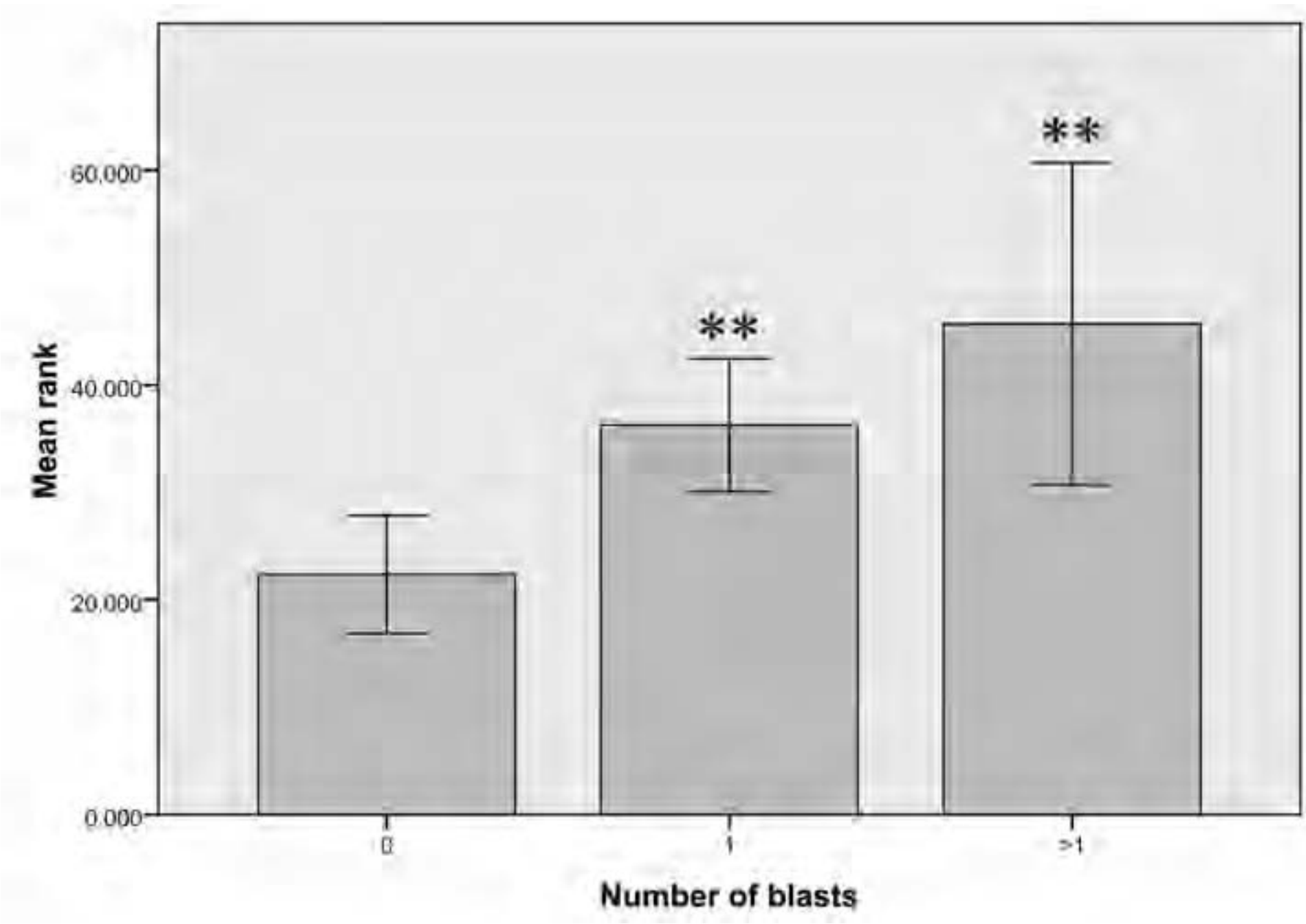

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CASE STUDY

Neuropsychological evaluation of blast-related concussion: Illustrating the challenges and complexities through OEF/OIF case studies

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Abstract

Background/objective: Soldiers of Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF) sustain blast-related mild traumatic brain injury (concussion) with alarming regularity. This study discusses factors in addition to concussion, such as co-morbid psychological difficulty (e.g. post-traumatic stress) and symptom validity concerns that may complicate neuropsychological evaluation in the late stage of concussive injury.

Case report: The study presents the complexities that accompany neuropsychological evaluation of blast concussion through discussion of three case reports of OEF/OIF personnel.

Discussion: The authors emphasize uniform assessment of blast concussion, the importance of determining concussion severity according to acute-injury characteristics and elaborate upon non-concussion-related factors that may impact course of cognitive limitation. The authors conclude with a discussion of the need for future research examining the impact of blast concussion (particularly recurrent concussion) and neuropsychological performance.

Keywords: *Traumatic brain injury, blast injury, neuropsychological injury*

Introduction

Mild traumatic brain injury (MTBI or concussion) occurs with alarming regularity in Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF) [1, 2]. Recent estimates suggest that between 12–23% of OEF/OIF personnel report a history of in-theatre concussion [3, 4] and as many as 300 000 OEF/OIF personnel may have sustained a combat-related concussion in the current conflicts [5]. Survey data suggest that blast represents one of the most common mechanisms of concussion in modern warfare [4, 6].

In this context, clinical neuropsychologists of the Veterans Affairs (VA) system are often called upon to evaluate whether OEF/OIF veterans' cognitive limitations reflect historical blast concussion(s). Neuropsychological evaluation of cognitive status in the wake of blast exposure can be challenging for a variety of reasons. In particular, clinicians may have difficulty assessing: (a) true concussion *severity*,

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(b) true concussion *frequency* and (c) the extent to which *non-concussion factors* may underlie long-term cognitive difficulties.

Difficulty assessing concussion severity often reflects limited knowledge of the blast events themselves. Information pertaining to blast exposure is commonly restricted to self-report months or years after the event(s). Understandably, veterans often show limited ability to describe acute-injury characteristics that accompanied the blast events. The accuracy of self-report regarding contextual issues, such as distance from the blast, is difficult to evaluate because primary records (e.g. Military Acute Concussion Evaluation [MACE; see www.DVBIC.org]) are often unavailable to VA providers. Concussion severity is conventionally rated according to acute-injury characteristics [1]. Thus, lack of reliable information regarding acute-injury characteristics makes it challenging to determine concussion severity and expected course of cognitive recovery.

Moreover, concussion severity cannot be reliably determined by endorsement of current post-concussive symptoms (PCS) on screening instruments as PCS are not necessarily specific to concussion. Fatigue, headache, dizziness and other PCS are common in healthy [7, 8] and non-TBI clinical samples [9]. Benge et al. [10], for example, found that PCS endorsed on the Neurobehavioural Symptom Inventory (NSI [11]) were strongly associated with issues unrelated to brain injury, such as post-traumatic stress. Other researchers have also raised concern that PCS may be more reflective of PTSD and other mental health issues [3, 4, 12] than concussion itself.

Neuropsychologists may also have difficulty assessing concussion *frequency*. Many OEF/OIF veterans report extended histories of blast exposure, sometimes spanning multiple deployments. Whereas a single uncomplicated concussion typically results in a favourable course of cognitive recovery within initial weeks or months [13–15], recurrent concussion may complicate recovery [16, 17]. Extensive blast exposure may obscure the ability to understand the extent to which cognitive limitations reflect a single concussion or the cumulative effect of multiple injuries. Also, not all blast exposures necessarily result in blast concussion.

To further complicate matters, blast events may be associated with *non-concussive factors* that affect cognitive performances. Blast may contribute to orthopaedic injuries [12] and pain that impact cognition. Blasts frequently give rise to post-traumatic stress. Survey data suggest that nearly one-half of OEF/OIF personnel who report a history of loss of consciousness also met criteria for post-traumatic stress disorder [12]. The deployment process itself, with or without blast exposure, may impact neuropsychological performances [18]. It is also conceivable that post-deployment stressors (e.g. re-adjustment to personal relationships, civilian employment) impact cognitive performances.

Secondary gain and response invalidity often complicate interpretation of neuropsychological test performances [19]. OEF/OIF personnel may submit claims of traumatic brain injury (TBI) to obtain service-connection income, which creates a clear incentive to embellish cognitive and psychological symptoms [20, 21]. In civilian samples, individuals with history of concussion evaluated in secondary gain contexts are more likely to show persisting cognitive symptoms than individuals evaluated in other settings [13]. Recent data suggest that OEF/OIF personnel with histories of concussion are also more likely to subvert neuropsychological test performance when evaluated in secondary gain settings [21], which further complicates the clinician's ability to determine the extent to which historical blast concussion may bear relevance on objective cognitive performances.

Thus, discriminating the source of cognitive impairment in the late stage of blast-related concussion is an inherently complex endeavour. The objective of the current study is to illustrate these challenges through presentation of three OEF/OIF blast concussion case studies to promote awareness of various non-concussive factors that may complicate interpretation of neuropsychological performances in the late stage of injury. Ultimately, it is the authors' hope that these case studies may assist the clinician to conceptualize potential source(s) of cognitive limitation in the wake of blast-related concussion and inform appropriate treatment recommendations.

Method and procedure

Assessment of blast concussion

In light of the high prevalence of blast concussion in the current military conflicts, the Departments of Defense (DoD) and Veterans Health Administration (VHA) have developed TBI screening instruments to identify veterans who may have sustained historical concussions [22]. The 'TBI Checklist', for example, is a mandated screening instrument administered within the VA system among returning OEF/OIF veterans [23]. Veterans with a 'positive' history of concussion according to the TBI checklist undergo more comprehensive evaluation via the 'TBI secondary level evaluation' [24].

During the TBI secondary evaluation, the clinician obtains information pertinent to the three most significant concussive events. The veteran is asked to

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approximate the year, month and date that the injuries were sustained. An estimate of proximity to blast(s) and whether additional factors may have mediated blast exposure(s) (e.g. utilization of protective gear; debris or shrapnel projected toward veteran) may be obtained. The veteran may be asked whether medical attention was provided (including administration of cognitive screening measures) and whether additional physical injuries were sustained. Most concussion rating criteria, including those presented by the American Congress of Rehabilitation Medicine (ACRM [25]), define injury severity according to loss of consciousness (LOC) and duration, post-traumatic amnesia (PTA) and duration and evidence of acute-injury neurologic symptoms or signs. As such, the veteran is asked to estimate duration of LOC, PTA and symptoms or signs (e.g. dizziness, headache) that may have been the direct result of concussion. Post-event information may be obtained to infer course of recovery (e.g. length of light duty; work accommodations). Obtaining information regarding whether peers were simultaneously injured as a result of blast may also assist in conceptualization of the blast event. Whenever possible, the provider attempts to corroborate self-report information with primary records (e.g. emergency medical documents; eyewitness accounts; Military Acute Concussion Evaluation [MACE; see www.DVBIC.org]) to further inform plausibility that concussion was sustained.

Minnesota Blast Exposure Screening Tool (MN-BEST)

The Minnesota Blast Exposure Screening Tool (MN-BEST; see Appendix) was developed by the current researchers to be used in conjunction with the TBI clinical reminder and TBI secondary level evaluations previously described. A primary rationale in developing the MN-BEST was to generate a single, composite numerical rating of one or more blast concussions. The current researchers reasoned that this single quantitative indicator may facilitate an expedient method of examining the cumulative effects of blast concussion and may be useful in optimally understanding and predicting functional outcomes (e.g. neuropsychological performances).

To complete the MN-BEST, the examiner first requests that the veteran estimate the total number of blast exposures experienced, whether or not they may have contributed to concussion. Next, consistent with the second level TBI evaluation [24], the veteran is asked to provide the date and location of the three most significant blast events. The three most significant events are assessed given evidence that risk of persisting symptoms increases following two or more concussions [16, 17].

For each of the three events, researchers offer an opinion as to whether historical blasts *plausibly* met a 'minimal biomechanical threshold' of concussion [26]. Those events that 'more likely than not' or 'likely' contributed to concussion are rated on a concussion severity continuum. This study has modified a rating scheme initially proposed by Ruff and Richardson [27] that includes three concussion severity classifications: Type I, II or III. Expanding upon this scheme, concussions contributing to neurologic symptoms in the absence of LOC or PTA are rated as 'Type 0' and assigned an overall blast-related TBI score of '1'. Type I concussions are assigned an overall blast-related TBI score of '2' and include 'altered state or transient loss of consciousness', PTA of no more than 60 seconds and one or more neurologic symptom. Type 0 and Type I concussions are considered to be consistent with ACRM [25] criteria. Type II and Type III concussions receive blast-related TBI scores of '3' and '4', respectively. Type II concussions consist of *definite* LOC of unknown duration to no more than 5 minutes, PTA from 60 seconds to 12 hours and at least one neurologic symptom. At the most severe end of the mild (uncomplicated) TBI spectrum, Type III concussions resemble criteria provided by the Diagnostic and Statistical Manual–Fourth Edition (DSM-IV [28]). Type III concussions consist of complete LOC for 5 to no more than 30 minutes, PTA greater than 12 hours and one or more neurologic symptoms. Mild complicated injuries, with indisputable evidence of structural injury, and moderate injuries (GCS 9–12; LOC no longer than 6 hours; PTA 1–24 hours [29, 30]) are assigned a severity score of '15'. Severe injuries (GCS 3–8; LOC > 6 hours; PTA > 24 hours [29, 30]) are assigned a score of '30'. Based upon this scheme, the total blast-related TBI score for mild uncomplicated blast-concussion ranges from 0 (no brain injury) to 12 (three Type III concussions). Inclusive of mild complicated, moderate and severe injuries, injury severity scores range from 0 (no brain injury) to 90 (three severe injuries).

It must be emphasized that the MN-BEST is a research instrument that was developed as a method of systematically describing historical blast concussions and their severity. Similar to the TBI clinical reminder and secondary TBI evaluation administered throughout the VA healthcare system [23, 24], the psychometric utility of the MN-BEST has yet to be comprehensively examined. Preliminary inter-rater reliability for the MN-BEST is encouraging. In a random sampling of MN-BEST concussion ratings from a sub-sample of 10 OEF/OIF veterans presented elsewhere [21], Cohen's alpha among the current research team was 0.98 ($p < 0.001$). Efforts are currently under way to identify MN-BEST

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validity with regard to convergence with diffuse tensor imaging (DTI) and electroencephalography (EEG) information. It is recommended that researchers and clinicians implement the MN-BEST cautiously and in conjunction with additional forms of information (e.g. in-theatre records; neuroimaging studies) until additional reliability and validity data has been successfully attained in sizeable blast concussion samples.

Case reports

The following case studies were obtained in three assessment settings: a research setting (Case A), clinical setting (Case B) and forensic setting (Case C). Case A was evaluated in the context of ongoing research studies at the Minneapolis VA Medical Center. Case B was evaluated in an extended rehabilitation Polytrauma inpatient setting and allowed for complete record review (including neuroimaging study). Case C was evaluated in the context of compensation and pension examination related to a claim of blast-related TBI. In compliance with regulations of the Minneapolis VA Medical Center, background information has been modified in the interest of protecting patient privacy.

Case A: An OEF/OIF veteran evaluated in a research context

Background.
Mr A is a 28-year old, Caucasian, married, right-handed, high school-educated, OEF/OIF veteran who presented for neuropsychological testing in the context of an ongoing research study at the Minneapolis VAMC. Mr A served as an Army infantryman for six years and recently completed multiple tours. He was discharged ~18 months prior to assessment. Mr A reportedly sustained six blast exposures during service in Iraq. He provided precise dates and locations for each event. PCS at the time of assessment included photophobia, tinnitus, irritability, headaches, sleep problems and diminished concentration. Mr A also disclosed that results of a recent compensation and pension evaluation supported 50% service-connection for PTSD. He was a full-time college student at the time of evaluation.

Blast event #1. The most significant blast event transpired in 2005, near a metropolitan area in Iraq. Mr A was an unrestrained passenger riding in the back of a Humvee when an artillery round exploded 15 feet away from the right side of the vehicle. He was wearing full body armour and a helmet. Shrapnel from the blast struck his right leg. The blast contributed to LOC for 20 seconds. PTA was minimal. Acute stage neurologic symptoms included headache, dizziness, disorientation, difficulty tracking, tinnitus, nausea, photophobia, phonophobia and imbalance. He continued to experience headache, tinnitus and dizziness for several hours after the event. He resumed usual military duties the day after the event. Mr A did not seek medical care following the blast. Shrapnel from the blast killed two peers who were travelling with him.

Blast event #2. The second-most significant blast transpired 1 week prior to Blast event #1. Mr A was standing in the cab of a Humvee. An IED exploded 25 feet behind the vehicle. Mr A was wearing full body armour and a helmet. He denied LOC, but did experience alteration of consciousness and disorientation. He denied PTA. He experienced headache and dizziness lasting a couple of hours, disorientation for 30 minutes, tinnitus for 24 hours, nausea for 1 hour and sensitivity to noise for 24 hours. He did not undergo medical care as a result of the blast. He maintained regular full-time military duties following the event. A peer lost his foot as a result of the blast.

Blast event #3. The third most significant blast event also occurred in 2005, ~4 months subsequent to the aforementioned events. Mr A was riding in the back of a heavily armoured vehicle when an IED exploded 500 metres to the left. He denied LOC or PTA. He experienced brief dizziness after the event but denied other neurologic signs. He denied that the event contributed to cognitive or functional difficulties.

Blast exposure assessment. On MN-BEST team consensus, each of these events was agreed to have been consistent with mild uncomplicated concussion. Event #1 was rated as a 'Type II' concussion given report of definite LOC between 1–60 seconds. Injury #2 was rated as a 'Type 0' concussion given no definite LOC or PTA, but acute-injury neurologic signs. Although external documents corroborating the events were not available, the consensus team agreed that it was 'more likely than not' that these two blast events contributed to concussion.

At face value, blast event #3 was classified as being most consistent with 'Type 0' concussion given a single neurologic sign (dizziness) and no evidence of LOC or PTA. Upon consensus, however, it was reasoned that brief dizziness was not necessarily indicative of concussion and may have represented transient autonomic changes or other non-concussion related factors. Blast #3 was therefore considered as 'less likely than not' to have caused a

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concussion and did not contribute to the overall Blast-related TBI score.

The overall MN-BEST Blast-related TBI score included event #1, which contributed a severity score of '3' and event #2, which contributed a severity score of '1'. Event #3 contributed a score of '0'. As such, the MN-BEST Total Blast-related TBI score amounted to '4'.

Neuropsychological assessment. Mr A completed a neuropsychological test battery that is routinely administered as part of an ongoing research project at the Minneapolis VA Medical Center (see Table I). Effort performances were within normal limits, suggesting that the profile represents an accurate reflection of cognitive functioning. Estimated level of pre-morbid intellectual ability was within the average range (WTAR FSIQ = 102). Performances on every measure administered, across the domains of simple attention, language, visual-spatial, executive, visual and verbal learning/memory functioning were within normal limits. In fact, Mr A demonstrated relative strengths on a number of tasks (e.g. visuoconstruction) that ranged from high average to superior.

Psychological assessment. Results of the Clinician-Administered PTSD Scale (CAPS [31]) supported formal PTSD diagnosis. Mr A described multiple traumatic events during deployments. Two peers were killed as a result of one blast event. Multiple additional combat-related events entailed threat of being killed. Mr A experiences intrusive thoughts when reminded of these events. He actively avoids triggers. He experiences sleep problems, irritability,

Table I. Neuropsychological profile for Mr A (research context).

Measure	Raw score	Standard score	Classification
Effort/Motivation			
VSVT (Easy, Hard, Total)	24, 24, 48	n/a	Sufficient effort
Rey FIT (Recall + Recog − FP)	30 (15, 15, 0)	n/a	Sufficient effort
CVLT-II Forced-Choice	16/16	n/a	Sufficient effort
Reliable Digit Span*	10	n/a	Sufficient effort
General Intelligence			
WTAR Pre-morbid FSIQ	35	SS = 102	Average
WAIS-III Information	18	SS = 12	High average
Attention/Concentration			
WAIS-III Digit Span (F/W)	17 (5/6)	SS = 10	Average
Language			
COWAT (FAS)	54	T = 59	High average
Visual-Spatial Function			
CFT Copy Trial	34	>16%ile	WNL
WAIS-III Block Design	61	SS = 15	Superior
Verbal Learning/Memory			
CVLT-II			
Trials 1–5 (Total)	59	$z = 0.9$	High average
Trial B	7	$z = 0.0$	Average
SF Recall	15	$z = 1.5$	Superior
SC Recall	14	$z = 1.0$	High average
LF Recall	14	$z = 1.0$	High average
LC Recall	15	$z = 1.0$	High average
Recog Disc	4.0	$z = 1.0$	High average
Visual Memory			
CFT 3′ Delay	29.5	86%ile	High average
Executive Function			
Trail Making Test A	16	T = 64	Superior
Trail Making Test B	48	T = 54	Average
WAIS-III Digit-Symbol	90	SS = 12	High average
Stroop Word	107	T = 50	Average
Stroop Colour	83	T = 52	Average
Stroop Colour–Word Interference	46	T = 51	Average

VSVT = Victoria Symptom Validity Test [39]; Rey FIT = Rey 15-Item Test [40]; WTAR = Wechsler Test of Adult Reading [41]; WAIS-III = Wechsler Adult Intelligence Scale – Third Edition [42]; COWAT = Controlled Oral Word Association Test [43]; CFT = Rey-Osterrieth Complex Figure Test [44]; CVLT-II = California Verbal Learning Test, 2nd edition [45]; Stroop = Stroop Colour and Word Test [46]; Normative data for Trail Making Test and COWAT were derived from Heaton et al. [47].
*After Greiffenstein et al. [34].

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hypervigilance and increased startle response. The Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID [32]) was suggestive of major depressive disorder in partial remission and alcohol dependence in remission. Validity scales from the Minnesota Multiphasic Personality Inventory–2nd edition (MMPI-2 [33]) were within normal limits (see Figure 1). The clinical profile was consistent with emotional distress, particularly paranoia, consistent with Mr A's ongoing symptoms of post-traumatic stress.

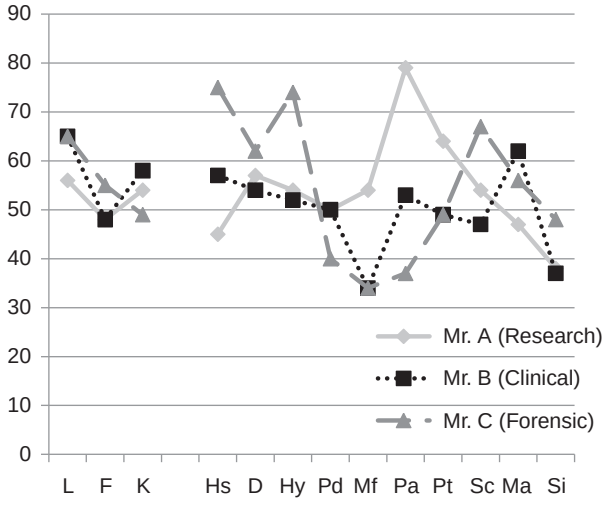

Figure 1. MMPI-2 profiles for three OEF/OIF personnel.

Conclusion. The MN-BEST disclosed two plausible blast-related concussions and a total blast-related TBI score of '4'. However, there was not evidence of cognitive impairment that might correlate with the history of blast-related concussions. Emotionally, Mr A continued to experience subtle paranoia and anxiety, consistent with the history of post-traumatic stress. As concerning as ongoing emotional difficulties may be, they did not clearly impact cognitive performances.

Case B: OEF/OIF veteran evaluated in a clinical VA polytrauma rehabilitation setting

Background. Mr B is a 40-year-old, Caucasian, right-handed, high school-educated, OIF Army infantryman referred for neuropsychological evaluation 3 months subsequent to blast exposure in Iraq. He sustained a penetrating left temporal brain injury secondary to projected shrapnel from an IED. There is indication of definite LOC of unknown duration. Mr B has no memory of the blast event and limited recall of being transported afterward. His first memory after the blast is 15 days later when he was aroused at a regional medical centre in Germany. It is unclear whether PTA was a manifestation of brain injury or related to intentional sedation. Computed tomography (CT) conducted in the acute-stage of recovery disclosed left temporal and parietal lobe contusions and a subdural haematoma with 4-mm shift. Repeat head CT conducted ~1 month after the initial study showed stable involvement of the left temporal and parietal lobes (see Figure 2).

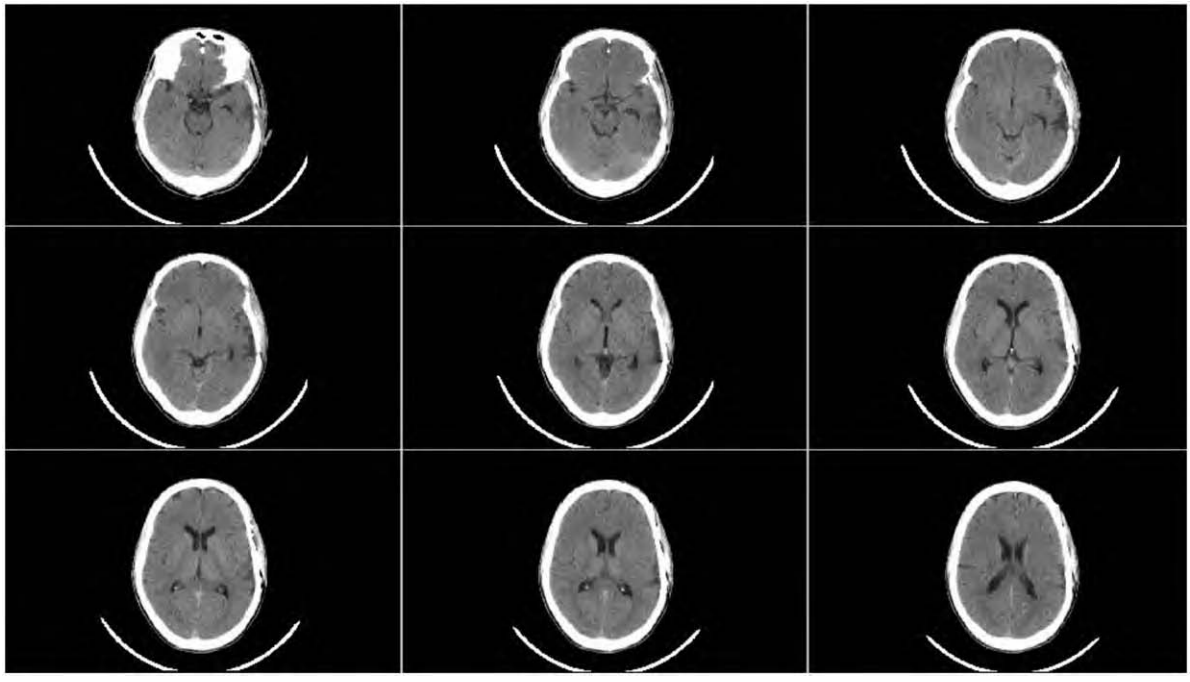

Figure 2. Conventional CT of Mr B's head depicting contusions to the left temporal lobe and portions of the left parietal lobe.

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At the time of evaluation, Mr B endorsed difficulty with word-finding and memory. Residual symptoms of blast exposure included imbalance, limited audition to the left side and dizziness with rapid movement. Mr B denied any history of psychiatric treatment. He denied any current symptoms of depression or anxiety but did acknowledge ongoing fatigue. He denied symptoms of post-traumatic stress.

Blast exposure assessment. The MN-BEST was not administered during the clinical evaluation, but was applied retrospectively by the current researchers. Duration of LOC could not be determined by self-report or record review. There appears to have been some period of PTA, although precise duration was obscured by what may have been intentional sedation soon after the injury. Upon arrival at a military medical unit soon after the injury GCS was 14/15. Records confirmed indisputable evidence of injury to portions of the left temporal and parietal lobes. Injury severity was consistent with a complicated, mild TBI. The consensus team determined plausibility of brain injury to be 'likely'. The nature of his mild complicated concussion was consistent with a composite MN-BEST rating of '15'.

Neuropsychological assessment. Table II presents neuropsychological test performances for Mr B. He demonstrated diminished effort on one embedded indicator (Reliable Digit Span [34]), but performances on other effort measures were within normal limits. Pre-morbid level of intellect was within the average range (WTAR FSIQ = 91) and is relatively consistent with available WAIS-III intellectual performances. Attention and concentration was variable, with diminished simple auditory attention and select impairments in visual and auditory sustained attention. Language, visual-spatial and motor performances were within normal limits. Executive functioning was variable, with select impairments in concept formation and cognitive efficiency (simple reaction time). Notably, visual and verbal learning/memory performances were within normal limits.

Psychological assessment. On the MMPI-2, Mr B responded defensively (see Figure 1). The profile was interpreted as under-estimating psychological and emotions symptoms and was interpreted cautiously. In general, there were no meaningful elevations on traditional clinical scales reflecting emotional distress. Mr B did endorse items in a manner that conveys a tendency to have difficulty expressing anger openly. Individuals with similar profiles tend to behave in an over-controlled manner and may have a history of behaving aggressively when their defenses are overtaxed (MMPI-2 Overcontrolled-Hostility Scale *T*-score = 69; MMPI = 2 Aggressiveness Scale *T*-score = 69).

Conclusion. In summary, Mr B clearly sustained a brain injury as a result of blast exposure. On MN-BEST consensus, it was agreed that he had sustained a mild complicated TBI (rating of '15'). Despite this, it is notable that he demonstrated intact performances in many areas of cognitive functioning. Impairments on select measures of attention and executive functioning were believed to be the direct result of brain injury. Consequently, it was reasoned that he would likely experience mild decrease in cognitive efficiency and problem-solving ability in complex, unfamiliar and demanding situations. Although Mr B appears to have adopted a defensive response style on the MMPI-2, there was not clear evidence of significant depression, anxiety or other psychological issues that would account for cognitive limitations.

Case C: OIF veteran evaluated in a forensic VA compensation and pension context

Background. Mr C is a 25-year-old, right-handed, Caucasian, married, high school-educated, OIF veteran with a history of blast exposure referred for compensation and pension examination related to claim of TBI while deployed to Iraq in 2007. He reports longstanding cognitive limitations attributed to this event. In addition to claims of TBI, medical records indicate Mr C is pursuing disability claims for 11 additional medical (e.g. bilateral loss of hearing; chronic back pain) and psychiatric (PTSD and depression) conditions. At the time of neuropsychological evaluation, he worked as a full-time carpenter.

Mr C was evaluated 8 months after an IED exploded ~20 feet away from his location. He was not wearing protective gear. He estimated that he was thrown 12 feet and rendered unconscious for ~5 minutes. He experienced minimal retrograde amnesia and ~20 minutes of anterograde amnesia. His first memory after the blast was being aroused by medical providers in a forward medical unit. He experienced dizziness, disorientation, headache, nausea and tinnitus for several hours after the event. After 2 weeks of light duty, he resumed usual infantry duties.

External records verified that Mr C was exposed to explosion/blast at the reported time and place. He was administered a brief concussion evaluation, the Military Acute Concussion Evaluation (MACE; see www.DVBIC.org), on three occasions: 2 hours, 2 days and 6 days post-injury. The MACE is derived

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Table II. Neuropsychological profile for Mr B (clinical context).

Measure	Raw score	Standard score	Classification
Effort/Motivation			
TOMM (Trial 1, Trial 2)	48, 50	n/a	Sufficient effort
WCST Regression*	−0.661	n/a	Sufficient effort
Reliable Digit Span +	3	n/a	Poor effort
General Intelligence			
WTAR Pre-morbid FSIQ	25	SS = 91	Average
WAIS-III Vocabulary	27	SS = 6	Low average
Attention/Concentration			
WMS-R Digit Span (F/W)	6 (4/3)	$z = -3.0$	Impaired
WAIS-III LN Sequencing	7	SS = 6	Low average
PASAT			
Trial 2.4s	29	$z = -3.72$	Impaired
Trial 2.0s	31	$z = -1.03$	Low average
Trial 1.6s	19	$z = -2.21$	Impaired
Trial 1.2s	20	$z = -1.19$	Low average
VIGIL			
K Omissions	0	$z = 0.47$	Average
K Commissions	2	$z = 0.14$	Average
K Reaction Time	426.6	$z = -0.55$	Average
AK Omissions	2	$z = -0.69$	Low average
AK Commissions	0	$z = 1.06$	High average
AK Reaction Time	452.8	$z = -1.74$	Impaired
Language			
WAIS-III Similarities	24	SS = 10	Average
COWAT (FAS)	32	T = 41	Low average
Animal Naming	26	T = 58	High average
Visual-Spatial Function			
WAIS-III Block Design	26	SS = 7	Low average
Verbal Learning/Memory			
WMS-R			
Logical Memory I	29	64%ile	Average
Logical Memory II	21	46%ile	Average
CVLT-II			
Trials 1–5 (Total)	47	$z = -0.3$	Average
Trial B	$z = 0.5$	Average	
SF Recall	12	$z = 0.5$	Average
SC Recall	12	$z = 0.0$	Average
LF Recall	13	$z = 0.5$	Average
LC Recall	13	$z = 0.0$	Average
Recog Disc	2.9	$z = -0.5$	Average
Visual Memory			
BVMT-R			
Trials 1–3 (Total)	28	T = 54	Average
Delayed Recall	10	T = 51	Average
Recognition Hits	6	>16%ile	WNL
Executive Function			
WCST			
Categories Completed	3	2–5%ile	Impaired
Total Errors	56	2%ile	Impaired
Persverative Errors	38	1%ile	Impaired
Failures to Maintain Set	1	>16%ile	WNL
Trail Making Test A	21	T = 56	Average
Trail Making Test B	52	T = 55	Average
WAIS-III Digit-Symbol	77	SS = 10	Average

(*continued*)

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Table II. Continued.

Measure	Raw score	Standard score	Classification
Stroop Word	98	T = 45	Average
Stroop Colour	68	T = 42	Low average
Stroop Colour–Word Interference	41	T = 46	Average
Motor Function			
Grooved Pegboard Dominant	73	T = 40	Low average
Grooved Pegboard Non-dominant	71	T = 48	Average

TOMM = Test of Memory Malingering [48]; WCST = Wisconsin Card Sorting Test [49]; WTAR = Wechsler Test of Adult Reading [41]; WAIS-III = Wechsler Adult Intelligence Scale – Third Edition [42]; WMS-R = Wechsler Memory Scale – Revised [50]; PASAT = Paced Auditory Serial Addtion Task [51]; VIGIL = VIGIL/W Continuous Performance Test [52]; COWAT = Controlled Oral Word Association Test [43]; CVLT-II = California Verbal Learning Test, 2nd edition [45]; BVMT-R = Brief Visuospatial Memory Test – Revised [53]; Stroop = Stroop Colour and Word Test [46]; Rey-O = Rey CFT = Rey-Osterrieth Complex Figure Test [44]; Normative data for Trail Making Test, Grooved Pegboard, Finger Tapping, Animal Naming, COWAT and BNT were derived from Heaton et al. [47]. *After King et al. [54]. +After Greiffenstein et al. [34].

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from the Standardized Assessment of Concussion (SAC [35]) and briefly assesses orientation, immediate memory, concentration and delayed memory. On initial MACE, Mr C reported sustaining LOC for seconds and a brief experience of PTA (seconds). He endorsed items of confusion, feeling dazed and tinnitus across the first two MACE administrations. During the third evaluation, he endorsed symptoms of headache, irritability, ringing of ears and difficulty concentrating. Initial MACE performance was 23/30. Subsequent MACE performances were 25/30 and 24/30, respectively. In light of acute-stage post-concussive symptoms and diminished cognitive performances, medical personnel provided a diagnosis of 'Concussion'.

Three months prior to neuropsychological evaluation, Mr C underwent secondary TBI examination [24] upon his return from deployment. Neurologic examination was normal, with the exception of low back pain and headaches. LOC at the time of the secondary TBI evaluation was reported to be '1 minute and 30 seconds' as a result of the blast. Mr C denied any experience of PTA. He endorsed 'moderate' to 'severe' PCS on the Neurobehavioural Symptom Inventory (NSI [11]).

Mr C also underwent mental health compensation and pension examination 20 days before neuropsychological evaluation. The blast event and an additional combat related-experience that involved the deaths of his peers were considered to represent plausible 'Criterion A' traumatic events [28], although additional diagnostic criteria for PTSD were not met. Mr C acknowledged that he was somewhat more irritable than usual since return from Iraq. He acknowledged that his cognitive limitations coincided with increased irritability and other emotional difficulties that he faced post-deployment. The examiner concluded that irritability, subtle emotional distress, and other activation symptoms were related to combat experiences. Findings supported Adjustment Disorder related to adjustment to post-deployment process.

Blast exposure assessment. The MN-BEST was not administered during the forensic examination but was applied retrospectively by the current researchers. Although discrepancies were noted over time regarding precise duration of LOC and PTA, the consensus team concluded that Mr C likely sustained a 'Type II' blast-related concussion. Plausibility of injury was supported by external records confirming definite brief LOC with brief PTA. Mr C also endorsed multiple neurological signs during the acute-stage of injury. MACE performances across the acute stage of injury were also diminished. This was consistent with a MN-BEST overall blast-concussion rating of '3'.

Neuropsychological assessment. Multiple effort performances were below expectation (see Table III), which suggests the neuropsychological profile is unlikely to represent an accurate reflection of Mr C's current cognitive functioning.

At face value, estimated level of pre-morbid intellectual functioning was within the average range (Barona Pre-morbid FSIQ = 108), while pro-rated level of intellectual ability was within the low average range (Pro-rated WAIS-III FSIQ = 84). Attention/concentration was generally intact, although recitation of digits was well below expectation. Language was variable, with impaired phonemic fluency. Visual-spatial performances were grossly intact. Executive performances were variable, with select impairments in cognitive efficiency. Visual memory was variable, with impaired delayed

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Table III. Neuropsychological profile for Mr C (forensic context).

Measure	Raw score	Standard score	Classification
Effort/Motivation			
TOMM (Trials 1, 2, 3)	23, 36, 38	n/a	Poor effort
VSVT (Easy, Hard, Total)	23, 15, 38	n/a	Poor effort
Rey FIT (Recall + Recog − FP)	18 (9, 9, 0)	n/a	Poor effort*
CVLT-II Forced-Choice	12/16	Cum % < 1	Poor effort
Finger Tapping DH	24.8	T = 12	Poor effort+
Reliable Digit Span	6	n/a	Poor effort†
General Intelligence			
WAIS-III Pro-rated FSIQ		84	Low average
Information	17	SS = 10	Average
Attention/Working Memory			
WAIS-III Digit Span (F/W)	11 (4/4)	SS = 6	Low average
WAIS-III Arithmetic	9	SS = 6	Low average
WAIS-III LN Sequencing	6	SS = 5	Impaired
Language			
WAIS-III Similarities	21	SS = 9	Average
COWAT (FAS)	19	T = 28	Impaired
Animal Naming	17	T = 39	Low average
BNT	54	T = 40	Low average
Visual-Spatial Function			
WAIS-III Matrix Reasoning	14	SS = 9	Average
WAIS-III Picture Completion	17	SS = 7	Low average
Verbal Learning/Memory			
WMS-III			
Logical Memory I	34	SS = 9	Average
Logical Memory II	19	SS = 9	Average
Logical Memory Recognition	22/30	n/a	Diminished
CVLT-II			
Trials 1–5	22	$z = -3.0$	Impaired
Trial B	4	$z = -1.0$	Low average
SF Recall	5	$z = -2.0$	Impaired
SC Recall	7	$z = -1.5$	Impaired
LF Recall	6	$z = -1.5$	Impaired
LC Recall	6	$z = -2.0$	Impaired
Recog Hits	7	$z = -5.0$	Impaired
Recog FP	1	$z = -0.5$	Average
Recog Disc	1.7	$z = -2.0$	Impaired
Visual Memory			
WMS-III			
Visual Reproduction I	72	SS = 6	Low average
Visual Reproduction II	64	SS = 10	Average
Visual Reproduction Recog	35	SS = 5	Impaired
Executive Function			
WMS-III Mental Control	16	SS = 5	Impaired
Trail Making Test A	35	T = 36	Impaired
Trail Making Test B	49	T = 52	Average
WAIS-III Digit-Symbol	55	SS = 7	Low average
Stroop Word	69	T = 31	Impaired
Stroop Colour	49	T = 52	Average
Stroop Colour–Word Interference	35	T = 40	Low average
WCST			
Categories Completed	6	>16%ile	WNL
Total Errors	32	19%ile	Low average
Perseverative Errors	18	12%ile	Low average
Failures to Maintain Set	1	>16%ile	WNL

(*continued*)

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Table III. Continued.

Measure	Raw score	Standard score	Classification
Motor Function			
Finger Tapping Dominant	24.8	T = 12	Impaired
Finger Tapping Non-dominant	23.0	T = 6	Impaired
Grooved Pegboard Dominant	95	T = 26	Impaired
Grooved Pegboard Non-dominant	97	T = 31	Impaired

TOMM = Test of Memory Malingering [48]; VSVT = Victoria Symptom Validity Test [39]; Rey FIT = Rey 15-Item Test [40]; WAIS-III = Wechsler Adult Intelligence Scale – Third Edition [42]; WMS-III = Wechsler Memory Scale – Third Edition [55]; CVLT-II = California Verbal Learning Test, 2nd edition [45]; BNT = Boston Naming Test [56]; COWAT = Controlled Oral Word Association Test [43]; Stroop = Stroop Colour and Word Test [46]; WCST = Wisconsin Card Sorting Test [49]. Normative data for Trail Making Test, Grooved Pegboard, Finger Tapping, Animal Naming, COWAT and BNT were derived from Heaton et al. [47]. *Based upon Boone et al. [40]; +Based upon Arnold et al. [57]; † Based upon Greiffenstein et al. [34].

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recognition of geometric figures. Verbal learning/memory was variable, with impaired delayed recognition of story details and select impaired trails in verbal list-learning and recognition.

Psychological assessment. On the MMPI-2 (see Figure 2), Mr C showed limited insight into psychological functioning and denial of minor shortcomings that most individuals are willing to acknowledge. The clinical profile suggested an experience of diffuse somatic symptoms, such as headaches, extreme pre-occupation with health, unusual sensory experiences and a subjective experience of cognitive limitation. Overall, the MMPI-2 profile is consistent with Mr C's endorsement of chronic low back pain and headaches described during the clinical interview.

Conclusion. Although Mr C appears to have sustained a blast-related concussion, the progressive cognitive decline described in the months following the blast event is inconsistent with the usual course of recovery following a single concussion. Cognitive limitations in the late stage of recovery are believed to reflect factors unrelated to brain injury (e.g. emotional difficulties related to post-deployment adjustment, chronic pain).

Results of neuropsychological evaluation suggest multiple indications of insufficient effort, which precluded an accurate understanding of Mr C's cognitive status. Select effort performances were well beneath what is observed, even among patients with significantly debilitating neurologic conditions such as dementia. At face value, the profile would suggest severe impairment across domains of cognitive function, which is inconsistent with a history of mild concussion and satisfactory work performance as a carpenter. There was enough evidence of insufficient effort to raise suspicion of *intentional* subversion of performance and, by at least one diagnostic scheme, the profile is consistent with criteria for Probable Malingered Neurocognitive Dysfunction [36].

General discussion

The above descriptions represent additions to the few case reports of OEF/OIF veterans with histories of blast concussion that have appeared in the clinical literature. The reports highlight complexities that often accompany interpretation of individual neuropsychological performances. Three OEF/OIF personnel, each with reasonably well-defined histories of blast exposure and concussion, exhibited unique patterns of cognitive performances and psychological profiles when evaluated in the late stage of recovery. These cases highlight several key points that clinical neuropsychologists should consider when evaluating OEF/OIF personnel with histories of blast concussion.

The case of Mr A illustrates the importance of simultaneous assessment of cognitive and psychological functioning among veterans presenting with persisting PCS. Mr A described two events that plausibly resulted in concussion. Subjective report of cognitive limitation was inconsistent with invariably intact neuropsychological performances. As such, ongoing subjective experience of cognitive difficulty was believed to be a manifestation of PTSD and emotional distress.

The serious nature of blast concussion is illustrated in the case of Mr B. Based upon what was known of the blast event, Mr B was likely to have sustained both the primary (direct) effects of the blast pressure wave, as well as secondary injury as a result of shrapnel that was lodged in the brain [2]. Head CT disclosed injury involving the left temporal and left parietal regions (see Figure 2). Overall

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history was believed to be consistent with a mild complicated brain injury. Given the serious nature of the injury, it was notable that Mr B demonstrated a variety of cognitive strengths on formal testing. On the other hand, he also showed a number of cognitive limitations (e.g. sustained attention, concept formation) that were believed to reflect residua of brain injury. The case of Mr B also bears relevance to a growing literature suggesting that 'mild' but complicated TBIs may follow a discrepant trajectory of cognitive recovery relative to mild uncomplicated concussions. Mild TBIs accompanied by visible structural injury may complicate recovery [26].

The remaining case study, Mr C, illustrates the importance of symptom validity assessment among OEF/OIF veterans with persisting PCS, particularly in forensic contexts [20, 21]. Mr C presented for neuropsychological evaluation in the context of a compensation and pension claim for TBI. It is likely that Mr C sustained a concussion related to blast exposure based upon information obtained through the clinical interview and external record review. Information directly relevant to the blast concussion in the form of serial MACE performances was helpful in determining plausibility of concussive injury. Although there was strong reason to believe that Mr C had sustained a blast-related concussion, he demonstrated numerous indications of insufficient effort on formal neuropsychological testing, which precluded a precise understanding of his cognitive strengths and weaknesses. In the context of secondary gain, the profile as a whole was consistent with probable malingered neurocognitive dysfunction [36].

The case of Mr C also illustrates that insufficient effort may be present simultaneously with documented history of concussion. In other words, brain injury and symptom exaggeration may co-exist [37]. Moreover, it should be noted that evidence of insufficient effort is not necessarily evidence of malingering. For some OEF/OIF veterans, variable task engagement may be associated with psychological distress, pain or sleep difficulty rather than deliberate subversion of performance [38].

Each of these case studies emphasized the importance of rating concussion severity according to acute-injury characteristics as opposed to current PCS. This study introduced the MN-BEST as one example of a systematic approach that may assist clinicians and researchers during the clinical inquiry process. Detailed accounts of the circumstances surrounding blast events may assist in determining whether it is plausible that a minimum biomechanical threshold of concussion was met [26]. It should be reiterated, however, that the MN-BEST was used as a research tool and, like the TBI clinical reminder [23] and second level TBI evaluation [24], the psychometric utility of the instrument is not yet fully understood. Ongoing studies are being conducted to examine whether MN-BEST scores are meaningfully related to white matter integrity on diffuse tensor imaging (DTI), electrophysiological function (EEG), psychological symptoms and neuropsychological function following blast-related concussion. Nevertheless, until the instrument can be correlated with acute-injury information, reliability and validity cannot be determined. It is strongly recommended that the MN-BEST be used cautiously until this additional psychometric data is obtained.

In conclusion, understanding the cognitive effects of blast concussion is vital given the unprecedented rate of injured soldiers in the current military conflicts. It has been the aim of this study to present just a few of the challenges that accompany neuropsychological evaluation of blast-related concussion in OEF/OIF personnel. Larger-scale empirical investigations are needed to clarify expected courses of recovery following isolated and recurrent blast exposure. Continued efforts to better understand how co-morbid non-concussive factors impact neuropsychological performances are also needed. Ultimately, clarifying the most probable source(s) of cognitive impairment, blast-related or otherwise, will inform treatment recommendations and ensure optimal care of OEF/OIF veterans.

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Appendix: Minnesota Blast Exposure Screening Tool (MN-BEST)

Appendix: Minnesota Blast Exposure Screening Tool (MN-BEST)

Patient Name _____ Date of Clinical Interview _____

A. Blast Exposures

A1. Estimated number of blast exposures (i.e. times the participant felt pressure wave from an explosion) _____

A2. Worst three blast exposures (i.e. greatest likelihood of injury to brain) - ***complete attached Table A1***

A3. Estimated total number of probable or definite blast-related **m**TBIs (complete after Table A1 is finished) _____

A4. Estimated total number of possible, probable, or definite blast-related **m**TBIs (complete after Table A1 is finished) _____

A5. Estimated total number of unlikely, possible, probable, or definite blast-related **m**TBIs (complete after Table A1 is finished) _____

A6. Estimated total number of probable or definite blast related TBIs (**moderate or severe**) (complete after Table A1 is finished) _____

Classification of mTBI (code TBI according to symptom of greatest severity)

	Type 0	Type I	Type II	Type III
LOC	Definite no LOC	Altered state (including dazed, confused, disoriented) or transient loss and unsure LOC	Definite loss with time unknown or < 5 minutes	Loss 5–30 minutes
PTA	Definite no PTA	1–60 seconds	60 seconds–12 hours	> 12 hours
Neurological symptoms	One or more	One or more	One or more	One or more

A1. Worst three BLAST EXPOSURES (i.e. greatest likelihood of injury to brain)

Event description	Date	LOC (dur)	PTA (dur)	Neurological sign(s)	TBI severity	mTBI type	Rating of certainty	Severity score (*if* Rating of certainty ≥ 2)
1.				Headache ___ Dizzy/Disor ___	Type: ___ Rationale:	Type: ___ Rationale:	Rating: ___ Rationale:	Rating: ___ Rationale:
Deployed: Y/N				Trbl Tracking ___ Tinnitus ___ Nauseous ___ Sens Light/Noise ___ Other _____ Comments:	Severity score: ___ Mild = 0 Mod* = 15 Sev = 30	Severity score: ___ Type 0 = 1 Type I = 2 Type II = 3 Type III = 4	0 = unlikely 1 = less likely than not 2 = more likely than not 3 = likely	
2.				Headache ___ Dizzy/Disor ___	Type: ___ Rationale:	Type: ___ Rationale:	Rating: ___ Rationale:	Rating: ___ Rationale:
Deployed: Y/N				Trbl Tracking ___ Tinnitus ___ Nauseous ___ Sens Light/Noise ___ Other _____ Comments:	Severity score: ___ Mild = 0 Mod* = 15 Sev = 30	Severity score: ___ Type 0 = 1 Type I = 2 Type II = 3 Type III = 4	0 = unlikely 1 = less likely than not 2 = more likely than not 3 = likely	
3.				Headache ___ Dizzy/Disor ___	Type: ___ Rationale:	Type: ___ Rationale:	Rating: ___ Rationale:	Rating: ___ Rationale:
Deployed: Y/N				Trbl Tracking ___ Tinnitus ___ Nauseous ___ Sens Light/Noise ___ Other _____ Comments:	Severity score: ___ Mild = 0 Mod* = 15 Sev = 30	Severity score: ___ Type 0 = 1 Type I = 2 Type II = 3 Type III = 4	0 = unlikely 1 = less likely than not 2 = more likely than not 3 = likely	
* Includes complicated mTBI						Total blast-related TBI Score: (0–90): _____		

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Evaluation Context Impacts Neuropsychological Performance of OEF/OIF Veterans with Reported Combat-Related Concussion

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Abstract

Although soldiers of Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF) encounter combat-related concussion at an unprecedented rate, relatively few studies have examined how evaluation context, insufficient effort, and concussion history impact neuropsychological performances in the years following injury. The current study explores these issues in a sample of 119 U.S. veterans (OEF/OIF forensic concussion, $n = 24$; non-OEF/OIF forensic concussion, $n = 20$; OEF/OIF research concussion, $n = 38$; OEF/OIF research without concussion, $n = 37$). The OEF/OIF forensic concussion group exhibited significantly higher rates of insufficient effort relative to the OEF/OIF research concussion group, but a comparable rate of insufficient effort relative to the non-OEF/OIF forensic concussion group. After controlling for effort, the research concussion and the research non-concussion groups demonstrated comparable neuropsychological performance. Results highlight the importance of effort assessment among OEF/OIF and other veterans with concussion history, particularly in forensic contexts.

Keywords: Forensic neuropsychology; Malingering/symptom validity testing

Introduction

Most studies examining the trajectory of cognitive recovery following mild traumatic brain injury (MTBI or concussion) include civilian samples, such as athletes who sustain sports-related injuries (e.g., McCrea, 2001). Although uncomplicated concussion frequently contributes to objective cognitive impairment within the acute stage of injury, the overwhelming majority of individuals attain a baseline level of functioning within days, weeks, to no more than a few months post-injury. This favorable course of recovery has been documented by several meta-analytic investigations (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Binder, Rohling, & Larrabee, 1997; Frencham, Fox, & Maybery, 2005; Iverson, 2005; Schretlen & Shapiro, 2003). Iverson aptly concludes, "under most circumstances, we should anticipate good recovery following MTBI" (p. 311).

Nevertheless, a minority of individuals experience persisting cognitive limitations and other post-concussive symptoms (PCS) beyond the usual course of recovery. Researchers have discussed various factors that may complicate recovery, such as premorbid psychological disturbance (Greiffenstein & Baker, 2001), co-morbid emotional difficulty (Moore, Terryberry-Spohr, & Hope, 2006), and chronic pain (Nicholson, 2000). Evaluation context has also been identified as a significant moderator of cognitive functioning following concussion (Belanger et al., 2005; Binder & Rohling, 1996). Belanger and colleagues (2005) illustrated that litigants and population-based samples showed similar cognitive limitations within the first 3 months post-injury ($d = 0.52$ vs. 0.63, respectively). However, whereas population-based samples showed essentially no cognitive limitations after 3 months ($d = 0.04$), litigants exhibited stable, or further diminished, cognitive

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performances ($d = 0.78$). In other words, individuals evaluated in a secondary gain context are more likely to exhibit ongoing cognitive limitations.

Rates of symptom exaggeration (e.g., insufficient effort) are known to increase dramatically in secondary gain contexts (AACN, 2007; Bush et al., 2005; Heilbronner et al., 2009). It follows that symptom exaggeration may partially explain why concussion groups evaluated in secondary gain contexts exhibit stable cognitive deficits beyond the typical recovery period. American Board of Clinical Neuropsychology members were surveyed to investigate rates of insufficient effort across clinical practices (Mittenberg, Patton, Canyock, & Condit, 2002). Respondents estimated that approximately 30% of personal injury and disability claimant groups exaggerate cognitive symptoms. Specific to head injury, respondents estimated that a much greater proportion of concussion groups exaggerate their symptoms (~39%) relative to moderate/severe brain injury groups (~9%).

Additional research illustrates the meaningful impact of insufficient effort on neuropsychological performance in forensic concussion samples. Green, Rohling, Lees-Haley, and Allen (2001) examined neuropsychological performance of a large forensic sample, 470 (52%) of whom had a history of concussion. The authors reported that concussion claimants with poor effort demonstrated significantly worse cognitive performances than claimants who had sustained moderate–severe brain injuries and exhibited sufficient effort on testing. Effort correlated highly ($r = 0.73$) with cognitive performance and accounted for 4.5 times more variance in overall cognitive performance than brain injury severity itself. In sum, there is clear evidence that evaluation of effort is crucial to the neuropsychological evaluation of late concussion, especially in secondary gain contexts.

Soldiers of Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF) sustain concussion at an unprecedented rate relative to previous conflicts (McCrea et al., 2008). Survey data suggest that between 12% and 23% of returning OEF/OIF personnel report a history of concussion (Hoge et al., 2008; Schneiderman, Braver, & Kang, 2008; Terrio et al., 2009). Increased report of concussion appears to reflect the novel features of modern warfare, such as frequent exposure to explosive blast. Although the civilian literature would suggest a favorable course of recovery for veterans with remote histories of concussion, a meaningful proportion of OEF/OIF veterans continue to report cognitive limitations and other PCS upon their return from deployment (Hoge et al., 2008). Few studies have examined how evaluation context and effort impact neuropsychological performances in OEF/OIF veterans with histories of concussion.

Regarding evaluation context, veterans with histories of concussion may initiate a service-connection claim and have incentive to embellish or exaggerate symptoms (Howe, 2009), even though this does not necessarily imply that they are malingering. Service connection is established through the compensation and pension (CP) process, which is similar to an independent medical examination or other civilian disability assessment. The CP process involves a claim of disability attributed to service-related injury (e.g., concussion). Neuropsychological evaluations conducted in the CP context may determine whether an OEF/OIF veteran's claim of concussion is associated with cognitive limitations. We are not aware of previous research examining neuropsychological profiles of OEF/OIF veterans in the CP context.

Regarding effort, most studies inclusive of OEF/OIF samples treat effort as a confounding variable without necessarily describing the effect on cognitive performance (Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009; Brenner et al., 2010; Vasterling et al., 2006). By including only those participants who demonstrate sufficient effort *a priori*, it is possible to explore research questions more effectively since the variance that would be attributed to poor effort is eliminated. For instance, in OEF/OIF samples with sufficient effort, researchers have examined whether blast and non-blast mechanisms of injury (Belanger et al., 2009), persisting symptoms following concussion (Brenner et al., 2010), or the deployment process (Vasterling et al., 2006) are associated with neuropsychological performance.

Only two published papers have focused explicitly on symptom validity testing and effort assessment in OEF/OIF samples. Armistead-Jehle (2010) examined Medical Symptom Validity Test (MSVT; Green, 2004) performance in a group of 45 OEF/OIF veterans with a history of concussion who underwent neuropsychological evaluation in a clinical context. Nearly 58% of the sample demonstrated insufficient effort on at least one MSVT indicator. Notably, the study did not summarize how effort impacted neuropsychological performance. A second study also focused on MSVT performance in 23 OEF/OIF veterans with historical concussion (Whitney, Shepard, Williams, Davis, & Adams, 2009). A significantly smaller percentage of individuals (17%) demonstrated insufficient effort on the MSVT and at least one other symptom validity test (e.g., Test of Memory Malingering; Tombaugh, 1996) or embedded effort indicator. Additional research with larger samples and a broader scope of effort measures is needed to determine the prevalence of insufficient effort among OEF/OIF veterans evaluated across various contexts.

The aim of the current study was to extend the symptom validity literature in OEF/OIF samples and clarify the impact of evaluation context, insufficient effort, and concussion on neuropsychological performances in the late stage of recovery (i.e., years post-concussion). The study explored three primary hypotheses. First, it was hypothesized that an OEF/OIF forensic concussion sample would demonstrate a higher rate of insufficient effort than an OEF/OIF research concussion sample, but a

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comparable rate of insufficient effort relative to a non-OEF/OIF forensic concussion sample. Second, regardless of context (forensic, research) or cohort (OEF/OIF, non-OEF/OIF), it was expected that insufficient effort would correlate significantly with overall cognitive performance. Third, when controlling for effort across OEF/OIF groups, it was predicted that individuals with a history of concussion would demonstrate comparable neuropsychological performances relative to those without concussion history.

Method

Participants

One-hundred and nineteen U.S. veterans participated in the current study (Table 1). All spoke English as a primary language and resided within the Midwestern region of the USA/Veterans Integrated Service Network (VISN) 23. Consistent with the general demographic makeup of this region, 111 (93.3%) were male and 111 (93.3%) were Caucasian. The mean age was 35.5 ($SD = 10.2$; range: 21–61 years). Most individuals obtained at least 12 years of formal education ($M = 13.7$; $SD = 2.3$; range: 6–21 years).

Participants were assessed in either a forensic CP ($n = 44$, 37%) or research ($n = 75$, 63%) context. Within the CP context, participants were consecutively referred for neuropsychological evaluation related to claim of concussion(s) sustained in service. Neuropsychological evaluation of these individuals was conducted by the first author. Research participants were OEF/OIF veterans recruited to participate in ongoing research activities at the Minneapolis VA Medical Center. Participants underwent neuropsychological assessment under the direction of the first, second, and third authors. The research sample was a subgroup of approximately 2,600 National Guard personnel deployed in 2005 for a 15-month tour in Iraq.

MTBI for the current sample was operationalized according to the criteria set forth by the American Congress of Rehabilitation Medicine (ACRM; Kay et al., 1993). Under this scheme, concussion is defined by the following criteria: (a) any period of loss of consciousness (LOC), (b) any loss of memory for events surrounding the event, (c) any alteration in mental state at the time of the accident, including feeling dazed, disoriented, or confused, and (d) focal neurologic deficits. By definition, LOC cannot persist beyond 30 min, and post-traumatic amnesia (PTA) cannot extend beyond 24 h.

Forensic context: OEF/OIF concussion group ($n = 24$). Nineteen (79.1%) of the OEF/OIF forensic participants endorsed a history of blast-related concussion, whereas the remaining five (20.9%) described concussions sustained by non-blast-related events (motor vehicle accident, fall-related). The mean number of reported concussions was 1.67 ($SD = 1.05$), with a median of 1.00 and a range of 1.00–4.00. Fifteen (62.5%) participants indicated that previous concussion resulted in alteration of consciousness, but denied that any of the concussions resulted in complete LOC or extended periods of PTA. Five (20.8%) endorsed neurologic signs, but denied that concussions resulted in any alteration of consciousness or PTA. Four (16%) indicated that concussions resulted in definite but brief LOC with minimal duration of PTA. A review of available medical records confirmed a psychiatric history that included post-traumatic stress disorder (PTSD) and other anxiety disorders ($n = 20$; 83.3%), major depressive disorder or depression not otherwise specified ($n = 9$; 37.5%), and/or alcohol abuse/dependence

Table 1. Demographics by evaluation context

Variable	Full sample ($N = 119$)		Evaluation context (M [SD])				F-value
			Forensic		Research		
	Range	M (SD)	OEF/OIF concussion ($n = 24$)	Non-OEF/OIF concussion ($n = 20$)	OEF/OIF concussion ($n = 38$)	OEF/OIF no concussion ($n = 37$)	
Age (years)	21–61	35.5 (10.2)	33.1 (9.9)	43.6 (12.6)[a,b,c]	34.4 (7.8)	33.9 (9.3)	5.72***
Education (years)	6–21	13.7 (2.3)	13.0 (2.1)	12.3 (1.8)[b,c]	14.5 (1.9)	14.1 (2.6)	5.54***
Concussions (number)	1–101	7.7 (16.9)	1.6 (1.0)[b]	2.2 (3.2)	14.5 (23.2)	n/a	6.37**
Most recent Concussion (weeks)	32–2,178	327.0 (425.6)	173.0 (83.6)	841.2 (614.1)[a,b]	149.1 (62.9)	n/a	36.70***

Notes: OEF = Operations Enduring Freedom; OIF = Operations Iraqi Freedom.
[a]Significantly different from Forensic OEF/OIF concussion sample.
[b]Significantly different from Research OEF/OIF concussion sample.
[c]Significantly different from Research OEF/OIF non-concussion sample.
**$p < .01$
***$p < .001$

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($n = 8$; 33.3%). One (4.2%) participant indicated a history of premorbid learning disability. Physical symptoms included ongoing headaches and/or other diffuse body pain attributed to previous military activities ($n = 22$; 91.7%). Three (12.5%) participants experienced ongoing tinnitus.

Forensic context: Non-OEF/OIF concussion group ($n = 20$). For the non-OEF/OIF concussion sample, seven (35%) participants completed tours from the Vietnam War era, and five (25%) completed tours during the Gulf War era. Eight (40%) participants sustained concussions as a result of military activities subsequent to the year 2000, but not in support of OEF/OIF. One non-OEF/OIF claimant (5%) endorsed a history of blast-related concussion during the time of service in Vietnam. The remainder of the non-OEF/OIF group described a history of non-blast-related concussions, such as motor vehicle accidents, boxing-related injuries, and concussions sustained as a result of falling. The mean number of reported concussions was 2.15 ($SD = 3.23$), with a median of 1.00 and a range of 1.00–15.00. Ten (50%) participants endorsed a history of definite LOC of brief duration with minimal PTA. Eight (40%) denied LOC, but indicated that concussions resulted in brief alteration of consciousness with minimal PTA. Two (10%) participants endorsed neurologic signs, but denied that concussions resulted in any alteration of consciousness or PTA. Medical records confirmed a psychiatric history of depression ($n = 10$; 50%), PTSD/other anxiety disorder ($n = 8$; 40%), and/or alcohol abuse/dependence ($n = 3$; 15%). Sixteen (80%) participants endorsed physical symptoms in the form of headaches or orthopedic pain.

Research context: OEF/OIF concussion group ($n = 38$). Thirty-eight research participants endorsed a history of blast-related concussion during service in Iraq or Afghanistan. The mean number of blast exposures was 14.5 ($SD = 23.20$), with a median of 4.00 and a range of 1.00–100. Sixteen (42.1%) denied that concussions were associated with LOC or PTA, but did describe neurologic signs. Twelve (31.6%) participants indicated definite but brief LOC associated with prior concussions, with brief PTA. Ten (26.3%) participants denied LOC, but indicated that concussions resulted in brief alteration of consciousness with minimal PTA and neurologic signs. According to the structured clinical interview for DSM-IV-TR Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 2007), psychiatric history for the research concussion group included major depressive disorder or depression not otherwise specified ($n = 17$; 44.7%), alcohol abuse/dependence ($n = 12$; 31.6%), and/or PTSD/other anxiety disorder ($n = 12$; 31.6%). Seventeen (44.7%) participants endorsed ongoing physical symptoms of headaches or other pain.

Research context: OEF/OIF non-concussion group ($n = 37$). Thirty-seven OEF/OIF research participants denied any history of combat-related concussion. SCID-confirmed psychiatric history included alcohol abuse/dependence ($n = 10$; 27.0%), major depressive disorder or depression not otherwise specified ($n = 8$; 21.6%), and/or PTSD/other anxiety disorder ($n = 9$; 24.3%). One participant (2.7%) endorsed history of possible learning disorder. Nine (24.3%) participants endorsed history of headaches and other physical pain ($n = 9$; 24.3%). Eight (21.6%) participants endorsed physical symptoms of headaches or other bodily pain.

Measures and Procedure

Neuropsychologists have developed a variety of symptom validity tests and symptom validity indices to evaluate response validity (Boone, 2007). Symptom validity tests, either forced-choice or non-forced-choice measures, are developed prospectively to assess effort and task engagement. Symptom validity indicators, either forced-choice or non-forced-choice, are derived from standard measures of cognitive ability.

Four effort measures were administered. Symptom validity tests included the Victoria Symptom Validity Test (VSVT; Slick, Hopp, Strauss, & Spellacy, 1996) and Rey-15 Item and Recognition Test (FIT; |Boone, Salazar, Lu, Warner-Chacon, & Razani, 2002). Symptom validity indicators included the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) Digit-Span subtest (Wechsler, 1997) and the California Verbal Learning Test-Second Edition (CVLT-II) Forced-Choice Recognition Trial (CVLT-II; Delis, Kaplan, Kramer, & Ober, 2000). "Insufficient effort" for each of these indicators was defined as follows. VSVT: Total Recognition <43 or Difficult Item Recognition <20 (Grote et al., 2000); FIT: Combination Score <21 (Boone et al., 2002); WAIS-III Digit Span: Reliable Digit Span <8 (Greiffenstein, Baker, & Gola, 1994); and CVLT-II: Forced Choice Recognition <15 (Delis et al., 2000).

Research participants completed a test battery to assess multiple domains of cognitive function (Table 2). General intelligence was assessed with the Information subtest of the WAIS-III. Attention was assessed with the WAIS-III Digit-Span subtest. Language and verbal fluency were assessed with Controlled Oral Word Association Test (COWAT; Gladsjo et al., 1999). Verbal learning/memory was assessed with the CVLT-II. Executive functioning and cognitive efficiency was measured by the Trail Making Tests A and B (TMT A and B; Heaton et al., 1991), Stroop Color Word Test (Golden, 1978), and the

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Table 2. Neuropsychological performances by evaluation context

Measure	Evaluation context (M [*SD*])				*F*-value	η^2
	Forensic		Research			
	OEF/OIF concussion ($n = 24$)	Non-OEF/OIF concussion ($n = 20$)	OEF/OIF concussion ($n = 38$)	OEF/OIF no concussion ($n = 37$)		
Effort/motivation						
VSVT						
Easy items	22.92 (2.00)[b,c]	23.55 (0.89)	23.90 (0.31)	23.89 (0.32)	5.90***	.13
Difficult items	15.63 (6.25)[b,c]	16.90 (5.51)[b,c]	22.11 (2.87)	23.24 (1.34)	24.95***	.39
Total items	38.54 (7.43)[b,c]	40.45 (5.94)[b,c]	46.00 (3.08)	47.14 (1.44)	24.02***	.39
Rey FIT						
Combination	26.13 (3.72)[b,c]	25.65 (5.26)[b,c]	28.84 (2.06)	29.35 (1.57)	10.14***	.21
CVLT-II						
Forced-choice	15.50 (1.18)	14.90 (1.97)[b,c]	15.87 (0.41)	15.92 (0.36)	5.34**	.12
WAIS-III						
RDS[+]	8.38 (1.71)	8.65 (1.60)	9.63 (1.98)	9.68 (2.06)	3.50	.08
Intellectual function						
WAIS-III						
Information (SS)	11.58 (1.82)	10.50 (3.46)	11.97 (1.92)	11.95 (2.30)	2.06	.05
Attention						
WAIS-III						
Digit Span (SS)	8.42 (2.77)	8.30 (2.34)	9.61 (2.55)	10.03 (2.67)	3.04	.07
Language						
COWAT (*T*)	42.83 (8.52)	45.60 (6.47)	44.79 (10.43)	45.97 (9.54)	0.61	.02
Verbal Memory						
CVLT-II						
Trials 1–5 (*T*)	46.33 (9.23)[c]	48.25 (10.39)	52.82 (8.61)	55.60 (8.57)	6.27***	.14
Long Free (*z*)	−0.73 (1.12)[c]	−0.48 (0.95)	0.03 (0.99)	0.30 (0.89)	6.84***	.15
Executive function						
TMT A (*T*)	39.96 (9.78)[b,c]	46.30 (9.72)	48.71 (10.44)	49.76 (11.25)	4.84**	.11
TMT B (*T*)	44.71 (10.22)[c]	47.45 (12.62)	51.45 (10.25)	52.84 (6.12)	4.23**	
Digit-Symbol (SS)	7.12 (2.53)[b,c]	6.95 (1.64)[b,c]	9.92 (2.53)	10.19 (2.61)	14.23***	.10
Stroop Word (*T*)	39.12 (7.54)[c]	39.40 (8.04)[c]	45.47 (9.01)	47.16 (8.97)	6.52***	.15
Stroop Color (*T*)	40.04 (7.00)[c]	37.45 (7.00)[b,c]	45.29 (8.60)	46.84 (7.10)	8.93***	.19
Stroop C-W (*T*)	43.78 (8.10)	41.15 (7.90)[c]	46.95 (9.09)	50.03 (8.93)	5.36**	.12
Effort Failures (Raw)	1.17 (0.87)[b,c]	1.15 (1.31)[b,c]	0.32 (0.58)	0.19 (0.46)	12.67***	.25
OTBM (*z*)	−0.75 (0.52)[b,c]	−0.64 (0.56)[b,c]	−0.15 (0.55)	0.02 (0.47)	14.72***	.28

Notes: OEF = Operations Enduring Freedom; OIF = Operations Iraqi Freedom; VSVT = Victoria Symptom Validity Test (Slick et al., 1996); Rey FIT = Rey 15-Item Test (Boone et al., 2002); WAIS-III = Wechsler Adult Intelligence Scale-Third Edition (Wechsler, 1997); COWAT = Controlled Oral Word Association Test (Gladsjo et al., 1999); CVLT-II = California Verbal Learning Test, Second Edition (Delis et al., 2000); Stroop = Stroop Color and Word Test (Golden, 1978); TMT = Trail Making Test (Heaton, Grant, & Matthews, 1991); OTBM = overall test battery mean performance (Green et al., 2001).
[b]Significantly different from Research OEF/OIF concussion sample.
[c]Significantly different from Research OEF/OIF non-concussion sample.
[+]After Greiffenstein et al. (1994).
**$p < .01$
***$p < .001$

Digit-Symbol Coding subtest from the WAIS-III. Although individuals evaluated in the forensic context completed a more extended neuropsychological test battery, analyses were conducted only on those measures that were administered uniformly across groups.

Similar to Green and colleagues (2001), an overall test battery mean (OTBM) of neuropsychological performances was generated. This was achieved by first transforming standard score performances (i.e., age-corrected scaled scores and *T*-scores) from 10 of the neuropsychological measures into *z*-scores, and then generating an average *z*-score across the measures. The WAIS-III Information subtest was used as an indicator of premorbid ability and did not contribute to the OTBM. OTBM was based on: WAIS-III Digit-Span and Digit-Symbol Coding (Scaled Scores), COWAT (*T*-score), CVLT-II Trials 1–5 (*T*-score), CVLT-II Long Free Recall (*z*-score), TMT A and B (*T*-scores), and Stroop Color Word Test (*T*-scores for Word, Color, and Interference trial) performances.

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Results

Preliminary analyses revealed significant differences for age, $F(3,115) = 5.72$, $p = .001$, and education, $F(3,115) = 5.54$, $p = .001$, across the four samples (Table 1). Tukey's HSD *post hoc* analyses revealed that the non-OEF/OIF forensic group was significantly older than the remaining three groups ($p < .005$). The non-OEF/OIF forensic group also completed significantly fewer years of education than the two research groups, $p < .05$. Neither age nor education was significantly correlated with overall number of effort failures. Education ($r = .23$, $p = .01$), but not age ($r = .11$, $p = .25$), was significantly correlated with overall neuropsychological performance.

Weeks since most recent concussion, $F(2,78) = 36.70$, $p < .0001$, and number of concussive injuries, $F(2,78) = 6.37$, $p < .01$, were significantly different across the three concussion groups. Tukey's HSD *post hoc* analyses revealed that the non-OEF/OIF concussion group reported a greater duration of time since most recent concussion relative to the OEF/OIF forensic and OEF/OIF research concussion groups ($p < .0001$). Additionally, the OEF/OIF forensic concussion group reported fewer previous concussions than the OEF/OIF research concussion group ($p < .01$).

To elucidate whether these factors were meaningful with regard to effort and neuropsychological performances, weeks since injury and number of concussions were correlated with the number of effort failures and the OTBM. These analyses revealed that weeks since most recent concussion was not significantly correlated with the number of diminished effort performances ($r = .19$, $p = .08$) or the OTBM ($r = -.11$, $p = .32$). The number of self-reported concussions was not significantly associated with the number of diminished effort performances ($r = -.20$, $p = .07$) or OTBM performance ($r = .15$, $p = .17$).

Table 2 presents effort and neuropsychological performances across the four samples. One-way analysis of variance (ANOVA) with group membership as the independent variable and effort as the dependent variable revealed that number of diminished effort performances was significantly different across the four groups—$F(3,115) = 12.67$, $p < .0001$. Tukey's HSD *post hoc* analyses revealed that both forensic groups demonstrated a greater number of diminished effort failures than research groups ($p < .0001$). Effort failures were not significantly different within contexts ($p > .05$).

On the individual effort measure level, ANOVA with group membership as the independent variable and performances on each of the effort measures revealed significant between-group differences on the VSVT Total items, $F(3,115) = 24.02$, $p < .0001$, VSVT Easy items, $F(3,115) = 5.90$, $p < .0001$, VSVT Difficult items, $F(3,115) = 24.95$, $p < .0001$, Rey FIT Combination score, $F(3,115) = 10.14$, $p < .0001$, and CVLT-II FC, $F(3,115) = 5.34$, $p < .01$). After correcting for multiple comparisons and assigning p-value to .01, RDS was not significantly different across groups, $F(3,115) = 3.50$, $p = .02$ and was not further investigated.

Tukey's HSD *post hoc* analyses revealed that both forensic groups showed significantly worse VSVT Total and Difficult item performances than both the research groups ($p < .0001$). The OEF/OIF forensic group showed significantly worse VSVT Easy item performance relative to both the research groups ($p < .0001$), whereas the non-OEF/OIF forensic group did not show these differences. VSVT performances were not meaningfully different between the OEF/OIF forensic and the non-OEF/OIF forensic groups ($p > .05$). *Post hoc* analyses revealed that both forensic concussion groups showed significantly worse Rey FIT Combination performance relative to both research groups, $p < .005$. Rey FIT Combination performances were not meaningfully different within contexts. *Post hoc* analyses revealed that the non-OEF/OIF forensic group showed significantly worse CVLT-FC performance relative to both research groups. CVLT-FC performance was not significantly different between the OEF/OIF forensic group and the two research groups, $p > .05$. CVLT-FC performance was not meaningfully different within contexts.

To further understand the impact of evaluation context on effort, rates of insufficient effort for each of three indicators (excluding RDS) were observed by evaluation context. Effort performances were comparable within contexts and justified creation of combined forensic ($n = 44$) and research ($n = 75$) groups. As shown in Fig. 1, 26 of 44 forensic participants (59.1%) showed at least one indication of insufficient effort, 7 of 44 (15.9%) showed two indications, and 4 of 44 (9.1%) showed three indications. In contrast, 8 of 75 (10.7%) research participants showed one indication of insufficient effort and 0% showed greater than one indication of insufficient effort.

Effort performances were also examined to identify the rates of insufficient effort on each individual measure. Of the 44 forensic participants, 26 (59.1%) demonstrated insufficient effort on the VSVT, whereas only six (8%) OEF/OIF research participants demonstrated insufficient effort on the VSVT. Seven (15.9%) forensic participants and two (2.7%) research participants showed insufficient CVLT-II FC performance. Four (9.1%) forensic participants demonstrated poor effort on the Rey FIT relative to 0% of the research sample.

Table 3 illustrates the magnitude of relationship between effort indicators and overall cognitive performance in the combined forensic and combined research groups, respectively. Effort and overall cognitive performance correlates were generally higher in the forensic group ($r = .45–.58$) relative to the research group ($r = .10–.29$). In other words, effort accounted for 20.3%–33.6% of the performance variance in the forensic group, compared with 1.0%–8.4% in the research group.

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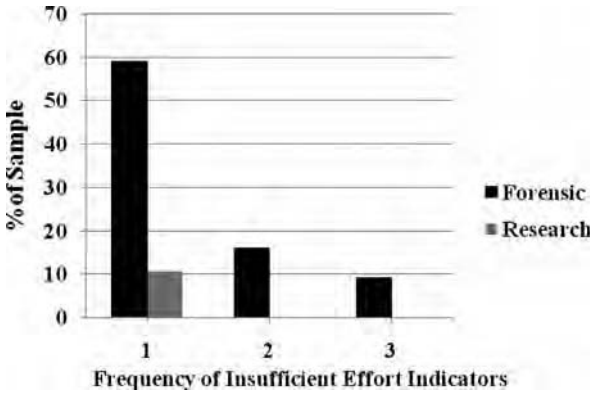

Fig. 1. Frequency of insufficient effort indicators by context. $N = 119$, including combined forensic ($n = 44$) and research ($n = 75$) samples. Effort indicators included VSVT (Slick, Hopp, Strauss, & Spellacy, 1996), Rey-15 FIT combination (Boone et al., 2002), and CVLT-II FC (Delis et al., 2000).

Table 3. Correlates of three effort measures and overall neuropsychological performance

Measure	VSVT	Rey FIT	CVLT-II	OTBM
VSVT	—	−.09	−.06	.29
Rey FIT	.57**	—	.28	.17
CVLT-II	.48**	.62**	—	.10
OTBM	.45*	.58**	.48**	—

Notes: Combined research sample ($n = 75$) depicted above the diagonal; Combined forensic sample ($n = 44$) correlations depicted below the diagonal. VSVT = Victoria Symptom Validity Test (Slick et al., 1996); Rey FIT = Rey 15-Item Test (Boone et al., 2002); CVLT-II = California Verbal Learning Test, Second Edition (Delis et al., 2000); OTBM = overall test battery mean performance (Green et al., 2001).
*$p < .01$
**$p < .001$.

Excluding OEF/OIF participants who displayed any indication of insufficient effort permitted unbiased assessment of whether concussion history impacted neuropsychological performance years after injury (Hypothesis 3). This resulted in 33 OEF/OIF participants with a history of concussion and 31 OEF/OIF participants without concussion with uniformly intact effort. Overall cognitive performance between these two groups was not significantly different—$t(62) = 1.63$, $p = .11$. However, it was noted that only five of the participants with concussion were derived from the forensic sample. Given concern that this limited number might not adequately represent OEF/OIF concussion samples evaluated in forensic contexts, neuropsychological performance comparisons were re-examined between the research concussion and the non-concussion groups. This resulted in identification of 28 research concussion participants and 31 non-concussion participants who demonstrated uniformly intact effort. As shown in Table 4, analyses did not yield any significant between-group differences across the neuropsychological measures examined nor on the OTBM performance.

Discussion

The aim of the current study was to explore the impact of evaluation context, insufficient effort, and concussion on neuropsychological performances in OEF/OIF veterans with varied concussion histories evaluated years following injury. As expected, in comparison to the research sample, OEF/OIF veterans with histories of concussion showed much higher rates of insufficient effort when evaluated in a forensic context. In contrast, the OEF/OIF forensic concussion sample demonstrated a similar rate of insufficient effort relative to a non-OEF/OIF forensic concussion sample. Insufficient effort, in turn, accounted for a significant proportion of variance in overall cognitive test performance in the forensic sample (from 20.3% to 33.6%), consistent with findings from civilian forensic concussion literature (Green et al., 2001; Rohling & Demakis, 2010). Insufficient effort was clearly less relevant to the research samples, and consequently did not show a meaningful association with overall cognitive performance (1.0%–8.4% variance accounted for by effort). After controlling for effort, OEF/OIF concussion and non-concussion groups did not show significant neuropsychological performance differences. The latter finding seems consistent with an extended civilian literature (Belanger et al., 2005; Binder et al., 1997; Frencham, Fox, & Maybery, 2005; Iverson, 2005; Schretlen & Shapiro, 2003) and a burgeoning OEF/OIF literature (Brenner et al., 2010).

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Table 4. Neuropsychological performances for OEF/OIF research concussion and non-concussion samples with uniformly sufficient effort

Measure	OEF/OIF research sample (*M* [*SD*])		*t*	*d*
	Concussion[a]	Non-Concussion[b]		
Intellectual function				
WAIS-III				
Information (SS)	12.21 (2.01)	12.26 (2.25)	0.08	0.22
Attention				
WAIS-III				
Digit Span (SS)	10.50 (2.29)	10.65 (2.37)	0.24	0.06
Language				
COWAT (*T*)	47.04 (8.94)	46.97 (9.69)	0.03	0.01
Verbal Memory				
CVLT-II				
Trials 1–5 (*T*)	54.43 (8.95)	57.16 (8.04)	1.24	0.32
Long Free (*z*)	0.27 (0.91)	0.45 (0.81)	0.82	0.21
Executive Function				
TMT A (*T*)	48.89 (9.89)	49.61 (11.66)	0.25	0.10
TMT B (*T*)	52.21 (10.20)	52.77 (5.83)	0.26	0.07
Digit-Symbol (SS)	10.46 (2.52)	10.35 (2.47)	0.17	0.04
Stroop Word (*T*)	46.29 (9.10)	48.58 (8.64)	0.99	0.26
Stroop Color (*T*)	46.00 (8.88)	47.26 (6.90)	0.61	0.16
Stroop Color-Word (*T*)	48.86 (9.35)	50.52 (9.22)	0.69	0.18
OTBM (*z*)	0.00 (0.55)	0.11 (0.42)	0.95	0.22

Notes: OEF = Operations Enduring Freedom; OIF = Operations Iraqi Freedom;WAIS-III = Wechsler Adult Intelligence Scale-Third Edition; COWAT = Controlled Oral Word Association Test; CVLT-II = California Verbal Learning Test, Second Edition; TMT = Trail Making Test; OTBM = Overall test battery mean (across 10 cognitive measures). All *t*-tests were non-significant.
[a]$n = 28$
[b]$n = 31$.

After controlling for evaluation context and relevant non-concussion-related factors (e.g., insufficient effort), remote history of concussion does not typically contribute to meaningful neuropsychological impairment in the late stage of recovery.

Merging current with previous OEF/OIF symptom validity research (Armistead-Jehle, 2010; Whitney et al., 2009), findings suggest that rates of insufficient effort clearly vary according to the setting in which veterans undergo assessment. In the current analysis, 22 of 99 (22.2%) OEF/OIF veterans demonstrated insufficient effort on the VSVT, a forced-choice effort measure. Six (8%) of these were research participants and 16 (66.7%) were forensic participants. In previously published investigations that include clinical OEF/OIF samples, results of forced-choice effort testing with the MSVT suggest that rates of diminished effort ranged from 17% (Whitney et al., 2009) to nearly 58% (Armistead-Jehle, 2010). Although it is acknowledged that classification accuracies may vary between the VSVT and the MSVT, available results suggest that 8% of OEF/OIF research participants, 17%–58% of clinical patients, and 67% of forensic claimants show insufficient effort on forced-choice measures. Cumulative findings suggest that response validity assessment is crucial in any evaluation context (including research), but particularly in forensic and clinical settings.

To be clear, these concerning rates of insufficient effort do not necessarily imply intentional subversion of performance (malingering). In fact, few of the current OEF/OIF forensic concussion participants demonstrated statistically less-than-chance level performance on forced-choice effort testing that would support a formal diagnosis of malingered neurocognitive dysfunction (Slick, Sherman, & Iverson, 1999). Among the 24 OEF/OIF veterans evaluated in the current forensic context, only three (6.8%) participants showed statistically less-than-chance level ($p < .05$) performance on the VSVT. For some OEF/OIF veterans, subtle variations in task engagement may reflect alternate explanations, such as emotional difficulty, pain, or fatigue (Vanderploeg & Belanger, 2009). At the same time, clinicians should recognize that most individuals with clinical conditions such as depression (Ashendorf, Constantinou, & McCaffrey, 2004) and pain (e.g., Etherton, Bianchini, Greve, & Ciota, 2005) perform very well on symptom validity testing. Confidence in assigning a diagnosis of malingering should increase in the presence of multiple indications of insufficient effort that are below established cut-scores (Larrabee, 2008).

It is also important to note that rates of insufficient effort were comparable in the non-OEF/OIF concussion sample and the OEF/OIF forensic concussion sample. Although additional data from larger samples are needed, current findings would suggest that cognitive response invalidity is a context-specific, not cohort-specific, phenomenon in veteran concussion samples. Veterans involved in disability claim related to a previous concussive injury are more likely to subvert performance, regardless of background, than those who undergo neuropsychological evaluation in other contexts.

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Findings also illustrate the differential utility of symptom validity tests. The OEF/OIF concussion groups in the current analysis were most likely to demonstrate insufficient effort on the VSVT, particularly on the difficult items. OEF/OIF veterans were far less likely to show diminished effort on the Rey FIT, CVLT-II FC, or RDS. In fact, RDS was not meaningfully different across groups, suggesting that it may have limited utility relative to other effort indicators. Clinicians should strongly consider employing the VSVT or other forced-choice effort measures during neuropsychological assessment of OEF/OIF concussion groups, particularly in forensic settings.

The current study is among the first to present relationships of multiple effort measures in the OEF/OIF forensic samples. Administration of multiple indicators essentially allows for a "continuous sampling" of effort throughout testing (Boone, 2009), and ultimately improves accuracy in the differential diagnosis of malingering (Bush et al., 2005; Larrabee, 2008; Nelson et al., 2003; Slick et al., 1999). This practice is only justified to the extent that effort measures are not redundantly correlated with one another (Rosenfeld, Sands, & van Gorp, 2000). As the VSVT, Rey FIT, and CVLT-II FC performances were significantly, but only moderately correlated with one another (Table 2), they may provide unique information with regard to task engagement. Future research could investigate incremental validity of multiple effort measures in veteran samples (e.g., Larrabee, 2008).

Present findings illustrate the non-specificity of PCS, which are common in healthy community samples (Paniak et al., 2002) as well as non-TBI clinical samples (Radanov, Dvorak, & Valach, 1992). For example, 21% of the current non-concussion research sample reported ongoing headaches and other forms of physical pain in spite of no reported history of concussion. This result would suggest that clinicians use caution in determining concussion severity on the basis of current PCS in OEF/OIF samples. Continued research is needed to identify factors that account for endorsement of persisting PCS (cf. Iverson, Lange, Brooks, & Rennison, 2010; Tsanadis et al., 2008) and PTSD (cf. Demakis, Gervais, & Rohling, 2008) in clinical neuropsychological evaluation settings. Greater understanding of co-morbid physical and psychological injuries may assist in conceptualization of subjective cognitive complaints and ultimately promote a "biopsychosocial approach" to treatment of persisting PCS (McCrea et al., 2009).

A limitation of the current study is that most OEF/OIF veterans sustained relatively few concussions, with most participants reporting only a single concussion as a result of combat activity. It is possible that samples sustaining more recurrent concussions would show greater cognitive compromise relative to non-concussion samples. Accumulating data suggest that recurrent concussion may be associated with a less favorable course of recovery relative to a single concussion and contribute to persisting cognitive limitation (Belanger, Spiegel, & Vanderploeg, 2010).

An additional limitation of this research is that we did not explore the impact of substance abuse/dependence, emotional factors, and other non-concussion-related variables on neuropsychological performances. This is significant because alcohol and other substances are known to have an untoward effect on cognitive functioning, and emotional distress in itself contributes to attention and other cognitive limitations independent of concussion history (e.g., Vasterling, Brailey, Constans, & Sutker, 1998; Vasterling et al., 2002). Future research is needed to identify how substance use, PTS, chronic pain, and other non-concussion-related factors impact cognitive performances across evaluation contexts. Additionally, the current study did not thoroughly explore the possibility that PTSD and concussion interact with one another to negatively impact cognitive outcomes. Future longitudinal research might document whether individuals with co-morbid PTSD and concussion demonstrate cognitive improvement with greater management of psychological difficulties.

In summary, this research suggests that rates of insufficient effort vary by evaluation context in OEF/OIF concussion samples. Consistent with civilian literature, insufficient effort accounts for a significant proportion of cognitive performance variance in forensic contexts. After controlling for evaluation context and insufficient effort, OEF/OIF veterans with remote history of concussion demonstrate similar cognitive performances relative to non-concussed veterans.

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Conflict of interest

None declared.

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Self-report of psychological function among OEF/OIF personnel who also report combat-related concussion

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Abstract

MMPI-2/RF profiles of 128 U.S. soldiers and veterans with history of combat-related concussion were examined. Participants evaluated in forensic (*n* = 42) and clinical (*n* = 43) settings showed significantly higher validity and clinical scale elevations relative to a research group (*n* = 43). In the full sample, a multivariate GLM identified main effects for: (a) disability claim status and (b) Axis I diagnosis across numerous MMPI-2/RF scales. Participants with co-morbid PTSD and concussion showed significant RC and SP scale elevations relative to those without Axis I diagnosis. Participants with PTSD and active disability claims were especially prone to elevate on FBS/FBS-r, and RBS. Implications for neuropsychologists who routinely administer the MMPI-2/RF in the context of combat-related concussion are discussed.

Self-report of psychological function among OEF/OIF personnel who also report combat-related concussion

Soldiers of Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF) are at great risk of sustaining combat-related concussion. In fact, some have suggested that rates of concussion in the current conflicts are unprecedented related to such factors as increased frequency of blast exposure, technologic advances that improve survival, and increased detection of concussive injury (McCrea et al., 2008). Although estimates vary, available data suggest that between 12 and 23% of soldiers may sustain concussion in support of the current conflicts (Hoge et al., 2008; Polusny et al., 2011; Schneiderman et al., 2008; Tanielian & Jaycox, 2008; Terrio et al., 2009).

A concerning number of OEF/OIF personnel continue to endorse persisting post-concussive symptoms (PCS) (e.g., irritability, tinnitus, balance problems, cognitive limitations) upon their return from deployment. Surveying a cohort of 2,525 U.S. infantryman three to four months after return from Iraq, Hoge et al. (2008) found that approximately 15% of the sample indicated a history of either loss or alteration of consciousness during deployment. Among those who indicated prior injury with either loss of consciousness or altered mental status, endorsement of persisting PCS ranged from 6.7 (17 of 254 endorsing ‘balance problems’) to 56.8% (67 of 118 endorsing ‘irritability’). However, after adjusting for emotional distress related to PTSD and depression, the overall effects of concussion were no longer associated with significant physical health outcomes. This research and other studies (e.g., Schneiderman et al., 2008; Terrio et al., 2009) suggest that persisting PCS are highly redundant with, and for many individuals best explained by, psychological and emotional difficulties. As Iverson and colleagues (2009) stated, “traumatic stress, life stress, depression, insomnia, chronic pain, marital and family distress, and substance abuse, singly or in combination, can be the proximate causes for these symptoms” (p. 1312).

In this context, thorough assessment of psychological and emotional functioning, as well as cognitive functioning, is essential to the clinical neuropsychological evaluation of OEF/OIF personnel with histories of combat-related concussion. Administration of comprehensive personality measures may assist in understanding the validity, quality, and severity of psychological and emotional symptoms.

The Minnesota Multiphasic Personality Inventory – Second Edition (MMPI-2; Butcher et al., 1989) continues to be one of the most frequently administered measures in clinical neuropsychological practice (Camara et al., 2000; Rabin et al., 2005). This popularity likely reflects the utility of the MMPI/MMPI-2 to detect psychological and emotional symptoms, as well as their veracity, in diverse neurologic and psychiatric samples. A briefer alternative to the MMPI-2, the MMPI-2 Restructured Form (MMPI-2-RF; Tellegen & Ben-Porath, 2008), has also become available for clinical use. The MMPI-2-RF contains revised versions of the MMPI-2 validity scales as well as a new validity scale designed to identify non-credible report of somatic symptoms (Fs), the Restructured Clinical (RC) scales, and newly developed Special Problem (SP) scales. The MMPI-2 RF provides a succinct overview of psychopathology and personality characteristics germane to neuropsychological assessments conducted in both clinical and forensic settings (Gervais et al., 2009.

Most MMPI/MMPI-2 concussion studies have been conducted in civilian samples. Studies conducted with the original MMPI (Leininger, Kreutzer, & Hill, 1991; Novack, Daniel, & Long, 1984) and MMPI-2 (Youngjohn et al., 1997; Thomas & Youngjohn, 2009) indicate that concussion samples with persisting symptoms are especially prone to elevate on scales associated with physical manifestations of emotional distress, such as the Hypochondriasis (*Hs*) and Hysteria (*Hy*) scales. Elevation patterns among RC scales in concussion samples also confirm this trend. For example, Thomas and Youngjohn (2009) found that concussion groups demonstrated the highest elevation on RC1 (Somatic Complaints), with lower elevations observed on scales associated with unusual

perceptual and thought processes, such as RC8 (Aberrant Experiences Scale). Disproportionate endorsement of somatic and other non-psychotic symptoms in concussion samples likely relates to the nature of persisting PCS, which include fatigue, dizziness, headache, tinnitus, and other nonspecific physical complaints.

MMPI studies have also demonstrated a 'paradoxical' severity effect between concussion samples and samples consisting of individuals who had sustained moderate or severe traumatic brain injuries (Kurtz et al., 2007; Miller & Donders, 2001; Thomas & Youngjohn, 2009; Youngjohn et al., 1997). Although concussion represents a milder form of brain injury, concussion samples with persisting PCS often show greater psychological distress on the MMPI-2 than groups with moderate or severe brain injuries. Importantly, most of these concussion samples were evaluated in the context of personal injury litigation, workers' compensation, or disability claim, suggesting that secondary gain often plays a role in symptom presentation. As such, it is important to develop MMPI-2/RF validity scales that are sensitive to symptom exaggeration in compensation-seeking concussion samples.

Recent reports on MMPI-2 response validity scales suggest that the Infrequency scale (F) and other 'F-family' scales (Infrequency Psychopathology, Fp; Back Infrequency, Fb; Dissimulation Index, F-K) show less utility in identifying symptom exaggeration in concussion samples relative to those intended to detect exaggerated somatic and cognitive symptoms (e.g., see Gervais et al., 2007). Three MMPI-2/RF validity scales that may be especially useful in this regard are the Symptom Validity Scale (previously known as Fake Bad Scale, FBS, Lees-Haley et al., 1991), Response Bias Scale (RBS; Gervais et al., 2007), and Infrequency Somatic Responses scale (Fs; Wygant et al., 2004). Regarding FBS, accumulating literature suggests that it is uniquely sensitive to 'somatic malingering' and insufficient effort on neuropsychological evaluation (Larrabee, 1998; Nelson et al., 2007, 2010; Ross et al., 2004; Slick et al., 1996). In a recent meta-analysis of MMPI-2 validity scales, FBS showed a very large effect size difference (Cohen's d = 1.28) in over-reporting traumatic brain injury

(predominately concussion) samples relative to comparison samples (Nelson et al., 2010). By contrast, F-family scales demonstrated more variable Cohen's *d* effect size differences, ranging from .22 to .78. In other words, concussion samples were most likely to show symptom exaggeration on FBS.

A 30-item revised version of FBS (FBS-r; Tellegen & Ben-Porath, 2008) was developed because the MMPI-2-RF does not include all of the original 43 FBS items. Although few studies have made use of concussion samples to examine the utility of FBS-r, the scale is likely to operate similarly to FBS given the extremely high correlations between the original and revised version reported in the MMPI-2-RF Technical Manual (*r*'s >.96) and comparable factor structures (Hoelzle, Nelson, & Arbisi, 2010). In one study, FBS-r showed utility with head injury samples; a large effect size (Cohen's *d* = 2.31) was observed between head injury controls and simulators, and strong classification accuracies were observed between T-80 and T-90 (Wygant et al., 2009).

The Response Bias Scale (RBS; Gervais et al., 2007) may also be useful in concussion samples. Unlike FBS, whose development entailed item selection on a 'rational' content basis for use in personal injury settings (Lees-Haley et al., 1991), RBS was developed with the explicit intention of identifying MMPI-2 items that were sensitive to insufficient effort on symptom validity testing. To accomplish this, Gervais and colleagues examined differential endorsement patterns of MMPI-2 items between individuals who had demonstrated sufficient versus insufficient effort on commonly employed effort tests (e.g., Word Memory Test, WMT, Green, 2003). The result was a 28-item scale that showed incremental prediction of effort performance above and beyond F, Fp, and FBS. Several follow-up studies, some of which included partial litigating concussion samples, have further supported use of RBS in forensic neuropsychological assessment (Gervais et al., 2008, 2009; Whitney et al., 2008; Wygant et al., in press). Cut scores between T-90 and T-100 were associated with strong classification accuracies (Wygant et al., in press). The latter authors conclude: "The RBS, by virtue of

its design and validation, is in a unique position among the other MMPI-2/MMPI-2-RF response bias indicators to provide compelling evidence of cognitive exaggeration, at least in disability settings."

Another recently developed validity scale that may be relevant to exaggeration of concussive symptoms is the MMPI-2-RF Fs (Wygant et al., 2004). Intended to identify unusual somatic complaints, Fs includes 16 items that were endorsed in 25% or less of two large diverse medical samples and a chronic pain sample (Tellegen & Ben-Porath, 2008). Wygant et al. (2009) reported a large effect size difference between head injury controls and head injury simulators on Fs (Cohen's *d* = .90). Cut-scores between T-90 and T-100 showed optimal classification accuracy in the latter study.

To summarize, the civilian literature suggests that concussion samples evaluated in secondary gain contexts are more likely to exaggerate psychological symptoms, and MMPI-2/RF scales associated with somatic and other non-psychotic symptoms (FBS/FBS-r, RBS, Fs) may be especially useful in detecting this. Civilian concussion samples are also prone to elevate on clinical scales sensitive to somatic (e.g., RC1) and other non-psychotic psychopathology.

To our knowledge there is only one study that has examined the MMPI-2 RF in soldiers exposed to concussive injuries. In a recent study of OEF/OIF veterans evaluated within six months after returning from a combat deployment to Iraq, no differences were found on any MMPI-2 RF validity or substantive scales between soldiers who screened positive for a concussion and those who did not (Arbisi, et al., in press).

The current study extends the use of MMPI-2/RF scales to a sample of OEF/OIF personnel with reported histories of combat-related concussion evaluated across forensic, clinical, and research settings. Three primary hypotheses motivated the analyses. First, we anticipated that the forensic sample would show significantly higher MMPI-2/RF validity scale elevations and a higher rate of response invalidity than the clinical and research groups, suggesting greater overall tendency to exaggerate psychological symptoms. Second, it was anticipated that the concussion samples would

show disproportionate elevations on FBS/FBS-r, RBS, and Fs relative to F-family scales, providing evidence of a greater tendency to over-report somatic/cognitive than psychotic symptoms in OEF/OIF concussion samples. Finally, it was anticipated that the current forensic and clinical groups would show significantly higher RC1 (Somatic Complaints) and MMPI-2-RF Special Problems Somatic/Cognitive scale elevations relative to the research group consistent with the quality of persisting PCS (i.e., physical, cognitive) in civilian concussion samples. Supplemental analyses were also undertaken to explore the impact of co-morbid Axis I diagnosis (e.g., PTSD) on MMPI-2/RF presentation.

Method

Participants and Procedure

Case files of 128 OEF/OIF veterans were retrospectively examined in the current study. Participants were evaluated in either a forensic (n = 42), clinical (n = 43), or research (n = 43) context. All resided within the Midwestern region of the United States within Veterans Integrated Service Network (VISN) 23. Consistent with the general demographic makeup of this region, 123 (96.1%) participants were Caucasian males. The mean age was 31.8 (SD = 8.6; Range 21 to 58 years) and most participants completed at least 12 years of formal education (M = 13.3; SD = 1.9; Range 6 to 21 years). Table 1 presents demographics across the three evaluation contexts.

Insert Table 1 about here

All participants reported a history of at least one combat-related traumatic brain injury that was no greater than mild in severity according to American Congress of Rehabilitation Medicine (ACRM; Kay et al., 1993) criteria. Individuals with histories of mild ‘complicated’ concussions, as indicated by demonstrable evidence of structural brain injury on neuroimaging, were not considered for inclusion.

The sample as a whole reported a mean of 3.4 combat-related concussions (*SD* = 4.4). On average, participants completed the MMPI-2 35.8 (*SD* = 18.5) months after most recent concussion. Forty-five (35.2%) participants indicated a history of definite, brief loss of consciousness as a result of previous combat-related concussion. Forty-nine (38.3%) participants endorsed a history of alteration without complete loss of consciousness. Thirty-four (26.6%) participants endorsed neurologic signs but denied that previous concussions resulted in any loss or alteration of consciousness.

The Forensic group consisted of 42 consecutively-referred OEF/OIF veterans who underwent neuropsychological evaluation as a component of compensation and pension examination (C & P) directly related to a claim of combat-related traumatic brain injury. C & P examinations resemble independent medical examinations or other administrative assessments conducted within the civilian forensic arena. The C & P claims board requests examiners to determine whether a history of concussion is etiologically linked with purported cognitive difficulties or reflects alternative factors (e.g., psychological distress, chronic pain, substance use). Record review revealed a psychiatric history significant for post-traumatic stress disorder (*n* = 20; 47.6%) or other anxiety disorder (*n* = 11; 26.2%), major depression (*n* = 13; 31.0%), adjustment disorder (*n* = 7; 16.7%), and/or substance abuse/dependence (*n* = 13; 31.0%). These diagnoses were provided by previous physicians and/or psychologists according to DSM-IV criteria and independent of current MMPI-2 profiles.

The Clinical group consisted of 43 consecutively-referred OEF/OIF personnel who underwent neuropsychological evaluation within a physical medicine and rehabilitation setting related to a history of concussion. Specifically, participants were evaluated through the Polytrauma rehabilitation network of the Minneapolis VAMC, one of four VA programs that specialize in the assessment and treatment of concussion and other physical difficulties subsequent to combat activity. Sixteen (37.2%) of the Clinical participants were retired veterans, 15 (34.9%) held active duty status, six (14.0%) were inactive ready reserve, and six (14.0%) were Army National Guard personnel. Review of records

disclosed a psychiatric history significant for post-traumatic stress disorder (*n* = 21; 48.8%) or other anxiety disorder (*n* = 9; 20.9%), major depression (*n* = 16; 37.2%), adjustment disorder (*n* = 7; 9.3%), and/or substance abuse/dependence (*n* = 11; 25.6%). Diagnoses were provided during previous evaluations by physicians and/or psychologists according to DSM-IV criteria, and independent of current MMPI-2/RF test results.

The Research group included 43 OEF/OIF veterans who were prospectively recruited to participate in an ongoing study that examines neuropsychological outcomes among OEF/OIF veterans with histories of concussion sustained during combat. The majority of the research participants deployed to Iraq as a single National Guard cohort in the spring of 2006 and completed a 15-month tour. A minority of the research sample completed multiple tours to Iraq and/or Afghanistan. Participants were evaluated with the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1990) and the structured clinical interview for DSM-IV-TR Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 2007), the results of which indicated histories significant for post-traumatic stress disorder (*n* = 17; 39.5%) or other anxiety disorder (*n* = 3; 7.0%), major depression (*n* = 21; 48.8%), and/or substance abuse/dependence (*n* = 15; 34.9%).

As shown in Table 1, significant group differences were observed in reports of LOC following concussion ($\chi_2(2) = 17.4$, $p = .002$), mean level of education in years (F [2,125] = 11.3, $p < .001$), and number of combat-related concussions (F [2,125] = 12.5, $p < .001$). However, none of these variables was significantly associated with any MMPI-2/RF validity or clinical scales independent of evaluation context. Frequencies of PTSD and other Axis I conditions were not significantly different across the three evaluation settings.

Measures

Each participant completed the MMPI-2 (Butcher et al., 1989) as a component of neuropsychological assessment related to a history of self-reported concussion. Profiles were initially

screened for excessive non-responding (Cannot Say > 30), acquiescence (True Response Inconsistency T > 80), and variable responding (Variable Response Inconsistency T > 80). RC scales were investigated as opposed to traditional MMPI-2 Clinical scales because the former remove nonspecific variance associated with demoralization (see Tellegen et al., 2003). The RC scales have improved psychometric properties and greater specificity to psychopathology relative to the Clinical scales (see Hoelzle & Meyer, 2008; Sellbom, Graham, & Schenk, 2006; Simms, Casillas, Clark, Watson, & Doebbeling, 2005). MMPI-2-RF Somatic/Cognitive scales included Malaise (MLS), Gastrointestinal Complaints (GIC) Head Pain Complaints (HPC), Neurological Complaints (NUC), and Cognitive Complaints (COG). These scales were examined as they may be especially relevant to the quality of persisting PCS. Additional MMPI-2-RF Internalizing Specific Problems (SP) Scales were also examined to further understand the emotional symptoms across contexts. These included Suicidal/Death Ideation (SUI), Helplessness/Hopelessness (HLP), Self-Doubt (SFD), Inefficacy (NFC), Stress/Worry (STW), Anxiety (AXY), Anger Proneness (ANP), Behavior-Restricting Fears (BRF), and Multiple Specific Fears (MSF).

Results

Table 2 illustrates significant between group differences for FBS ($F[2,125] = 17.51$, $p < .001$), FBS-r ($F[2,125] = 16.80$, $p < .001$), RBS ($F[2,125] = 8.15$, $p < .001$), and F-r ($F[2,125] = 5.84$, $p < .005$). Tukey HSD post-hoc analyses revealed that the forensic group produced significantly higher elevations on FBS ($p < .001$), FBS-r ($p < .001$), RBS ($p = .001$), and F-r ($p = .01$) relative to the research group, with effect size differences ranging from moderate to large ($d = .57$ to 1.21). Post-hoc analyses also revealed that the clinical group produced significantly higher elevations on FBS ($p < .001$), FBS-r ($p < .001$), RBS ($p = .004$), and F-r ($p = .004$) relative to the research group, with effect size differences ranging from moderate to large (Cohen's $d = .64$ to 1.11). Post-hoc analyses did not reveal any significant validity scale differences between the forensic and clinical groups.

Insert Table 2 about here

Table 2 also presents MMPI-2 RC scales and MMPI-2-RF SP scales in the three samples. For the RC scales, between-group differences were noted for RCd (F [2,125] = 7.27, p =.005), RC1 (F [2,125] = 11.66, p < .0001), and RC2 (F [2,125] = 10.47, p < .0001). Post-hoc analyses revealed that the forensic group showed significantly higher elevations on RCd (p = .005), RC1 (p < .001), and RC2 (p = .003) relative to the research group, with large effect size differences noted (Cohen's d >.70). The clinical group also showed significantly higher elevations on RCd (p = .002), RC1 (p = .001), and RC2 (p < .001) relative to the research group. RC scales were not significantly different between the forensic and clinical groups.

For the MMPI-2-RF SP scales, between-group differences were noted for MLS (F [2,125] = 11.2, p < .001), GIC (F [2,125] = 5.1, p =.007), HPC (F [2,126] = 11.4, p < .001), NUC (F [2,125] = 9.7, p < .001), COG (F [2,125] = 6.9, p < .001), and STW (F [2,125] = 6.08, p < .01). Post-hoc analyses revealed that the forensic group elevated more significantly than the research group on MLS (p = .003), GIC (p = .01), HPC (p < .001), NUC (p = .001), and COG (p = .001). The clinical group also showed significantly higher elevations on MLS (p < .001), HPC (p = .001), NUC (p = .001), COG (p = .005), and STW (p = .001) relative to the research group. MMPI-2-RF SP scales were not significantly different between the forensic and clinical groups.

Evidence of statistically significant validity scale differences between groups does not necessarily translate to *clinically* meaningful differences. Inspection of individual validity scales is needed to identify frequency of potential symptom exaggeration according to designated cut-scores (Ben-Porath & Tellegen, 2008; Butcher et al., 2001; Graham, 2005; Greiffenstein et al., 2007; Tellegen & Ben-Porath, 2008; Wygant et al., 2009). Table 3 presents rates of possible symptom exaggeration on

MMPI-2/RF validity scales across evaluation contexts according to various cut-scores. For those scales that were statistically significant across evaluation context (FBS, FBS-r, RBS, and F-r), a sizeable proportion of the forensic and clinical groups showed potential symptom exaggeration on *FBS* (52.4 to 53.5% at T > 79; Greiffenstein et al., 2007), *FBS-r* (38.1 to 46.5% at T > 79; Ben-Porath & Tellegen, 2008), *RBS* (25.6 to 31.0% at T > 89; Wygant et al., in press), and F-r (19.0 to 23.3% at T > 89; Ben-Porath & Tellegen, 2008). Symptom exaggeration was far less frequent on these scales in the research group (ranging from 4.7 to 9.3%).

Insert Table 3 about here

Supplemental analyses were conducted to further understand why similar frequencies of symptom exaggeration may have been observed across forensic and clinical groups. Unlike the forensic group, the clinical and research groups were not evaluated in a context that is explicitly associated with secondary gain. Nevertheless, it was reasoned that clinical participants with pending disability claims may have presented differently than those without pending claims and retrospective exploration of service-connection status was therefore conducted. Cross-tabulation of evaluation context (clinical or research) by service-connection status (active versus non-active claims) was significant [$\chi_2(1)= 11.06$, $p = .001$]. Specifically, a greater number of the clinical participants ($n = 24$; 55.8%) indicated that they were involved in a pending compensation/pension claim relative to the research participants ($n = 9$; 20.9%). This suggests that the higher rate of symptom exaggeration on MMPI-2/RF validity scales in the clinical sample may relate to increased involvement in disability claims. Additionally, although Axis I diagnostic frequencies were not significantly different across evaluation contexts (see Table 1), it was reasoned that forensic and clinical participants with co-morbid

histories of concussion and PTSD may have presented differently on MMPI-2/RF scales relative to those with other co-morbid Axis I conditions or no co-morbid psychological diagnosis.

With these considerations in mind, an 'active claim' group consisting of forensic participants and those clinical participants with active disability claims (n = 66), was developed. A 'non-active claim group' was also developed and included clinical and research participants without active disability claims (n = 53). The nine research participants who acknowledged pending disability claims were not included in the secondary gain sample because they were informed through the initial research consenting process that their MMPI-2/RF results would not have bearing on any services for which they might be eligible. An Axis I diagnosis variable was also developed, and consisted of participants with PTSD (alone or in conjunction with additional psychological condition), those with other Axis I condition (non-PTSD), and those without any Axis I condition. Frequencies of active versus non-active disability claims were not significantly different across the latter three diagnostic groups [$\chi_2(2)$= 3.28, p = .20].

Multivariate general linear modeling (GLM) was conducted with disability claim status (active or not active) and Axis I diagnosis (PTSD+, Other Axis I, None) as class variables, and MMPI-2/RF scales as dependent variables. Three separate models were conducted, one that included validity scales as dependent variables, one with RC scales as dependent variables, and one with SP scales as dependent variables. After correcting for multiple comparisons ($p \leq .001$), respective analyses resulted in significant overall models for many of the MMPI-2/RF scales. Fp (F[5, 118] = 1.18; p = .323) and Fp-r (F[5, 118] = 1.18; p = .021) were the only two validity scales that did not show significance. Among the RC and SP scales, RCd (F[5, 118] = 7.35; p = <.001), RC1 (F[5, 118] = 7.33; p < .001), RC2 (F[5, 118] = 6.45; p < .001), MLS (F[5, 118] = 9.80; p <.001), GIC (F[5, 118] = 4.91; p <.001), HPC (F[5, 118] = 6.83; p <.001), COG (F[5, 118] = 7.43; p = <.001), STW (F[5, 118] = 6.37; p

<.001), AXY (F[5, 118] = 5.93; p <.001), and ANP (F[5, 118] = 5.91; p <.001) all reached significance within respective models.

GLM revealed main effects for disability claim status and Axis I diagnosis on a variety of MMPI-2/RF scales. Regarding disability claim status (see Table 4), after correcting for multiple comparisons ($p \leq .001$), FBS-r (F[1, 118] = 11.80; p <.001) was the only validity scale to show a statistically significant main effect between those with and without active disability claims, though FBS (F[1, 118] = 10.22; p = .002) and RBS (F[1, 118] = 6.63; p = .011) showed near significance. No main effect for disability status was observed for the RC scales, though RC1 (F[1, 118] = 9.79; p = .002) showed near significance. Among the SP scales, MLS, GIC, HPC, COG, STW, AXY, and ANP were all significantly higher among those with active disability claims relative to those without active claims.

Insert Table 4 about here

Table 5 depicts MMPI-2/RF scales by Axis I diagnosis. Among the validity scales, a main effect for Axis I diagnosis was observed for F, F-r, Fb, FBS, FBS-r, and RBS. Post-hoc analyses revealed that the PTSD+ group showed significantly higher elevations on these scales relative to those without Axis I conditions. Among the RC scales, a main effect or Axis I diagnosis was observed for RCd, RC2, RC4, and RC7, with significantly higher elevations noted between the PTSD+ and no Axis I diagnosis groups. Those with Other Axis I conditions also showed significantly higher elevations relative to those without Axis I conditions on RC2. For SP scales, a main effect for Axis I was observed for MLS, GIC, COG, SFD, STW, AXY, and ANP, with the PTSD+ group showing significantly higher elevations relative to those without an Axis I condition. MLS and COG were also significantly higher in the Other Axis I group relative to those without Axis I condition.

Insert Table 5 about here

Multivariate GLM did not reveal significant interaction effects across any MMPI-2/RF scales, though a near interaction effect was observed for FBS (F[2, 118] = 4.10; p = .019) and FBS-r (F[2, 118] = 2.60; p = .079). Table 6 shows MMPI-2/RF presentations by disability claim status and co-morbid Axis I diagnosis.

Insert Table 6 about here

To further understand frequencies of possible symptom exaggeration in the current sample, MMPI-2/RF validity scale frequencies were examined at various cut-scores (see Table 7). Overall, participants with active disability claims showed more frequent validity scale elevations than those without claims. For those validity scales that were noted to be significantly impacted by Axis I conditions (see Table 5), odds ratios were generated across the validity scales using previously recommended cut-scores suggestive of possible symptom exaggeration (FBS raw score of >25 [T > 79], Greiffenstein et al., 2007; FBS-r T >79, Ben-Porath & Tellegen; RBS T > 89, Wygant et al., in press; F-scale T > 89, Fb T > 89, Butcher et al., 2001; and F-r T > 89, Ben-Porath & Tellegen, 2008). Results indicated that participants with active disability claims, across all Axis I diagnosis groups, were approximately four times more likely to elevate on FBS [$\chi^2(1)$= 11.7, p = .001; OR = 3.86, 95% CI = 1.73-8.63)], and approximately three times more likely to elevate on FBS-r [$\chi^2(1)$= 5.64, p = .018; OR = 2.64, 95% CI = 1.16-6.04)] and RBS [$\chi^2(1)$= 5.91, p = .015; OR = 3.07, 95% CI = 1.19-7.92)] relative to OEF/OIF personnel without disability claims. Chi-squares were not statistically different for the remaining validity scales between participants with and without active disability claims.

Insert Table 7 about here

Among the participants with previously diagnosed PTSD, those with active claims were nine times more likely to elevate on FBS [$\chi_2(1)= 14.37$, $p < .0001$; OR = 9.0, 95% CI = 2.62 to 30.87], approximately five times more likely to elevate on FBS-r [$\chi_2(1)= 8.39$, $p = .004$; OR = 5.64, 95% CI = 1.59 to 20.02], and approximately five times more likely to elevate on RBS [$\chi_2(1)= = 7.29$, $p = ,.007$; OR = 5.61, 95% CI = 1.41 to 22.40] than those without active claims. Chi-squares were not statistically different for the remaining validity scales in the PTSD active and non-active claim groups.

Discussion

The current study examined MMPI-2/RF profiles of OEF/OIF personnel who underwent neuropsychological evaluation of concussion across forensic, clinical, and research contexts. As expected, the forensic group demonstrated significantly higher elevations on MMPI-2/RF validity scales than the research group. Consistent with previous research in non-OEF/OIF samples (Nelson et al. 2010; Gervais et al., 2008), forensic and clinical OEF/OIF samples with reported histories of concussion are most likely to elevate on validity scales designed to detect exaggeration of somatic (FBS/FBS-r) and cognitive (RBS) symptoms, though they may also elevate on validity scales sensitive to exaggeration of general psychopathology (F-r). Across evaluation contexts, OEF/OIF disability claimants were approximately four times more likely to show possible exaggeration on FBS and approximately three times as likely to exaggerate on FBS-r and RBS relative to personnel without disability claims. Similar to civilian concussion samples (Thomas & Youngjohn, 2009; Youngjohn et al., 1997), OEF/OIF concussion samples typically elevated on clinical scales associated with somatic preoccupation (RC1), emotional demoralization/depression (RCd, RC2), and difficulties associated with health and cognitive function (MLS, HPC, NUC, COG).

However, results indicate that across evaluation contexts, MMPI-2/RF presentation clearly varies by co-morbid Axis I diagnosis. In particular, participants with previously diagnosed PTSD showed significant elevations on multiple scales that may reflect a history of psychological distress, persisting post-concussive symptoms, or both. Significant elevations on various RC scales (e.g., RCd, RC2, RC4, and RC7) and SP scales (e.g., AXY, ANP) seem very much consistent with hallmark symptoms of post-traumatic stress. Other elevations (e.g., RC1, COG), however, could be more suggestive of persisting post-concussive symptoms in these groups (e.g., somatic complaints, cognitive limitations).

This heterogeneous pattern of symptom presentation seems consistent with the findings of Arbisi et al. (in press), who examined profiles of four OEF/OIF groups: PTSD only, concussion only, co-morbid PTSD/concussion, and neither PTSD nor concussion. The authors found that 'conceptually related scales', including RC7 were effective in identifying PTSD. However, the authors also found that "MMPI-2 RF scales associated with somatic concerns were also significantly elevated in the PTSD group suggesting that beyond symptoms commonly associated with PTSD, veterans returning from the war in Iraq who screen positive for PTSD report poor health and a range of somatic concerns." Taking these findings together with current findings, it appears that individuals with co-morbid PTSD and concussion tend to show a more complex pattern of symptom presentation on the MMPI-2/RF than individuals with either condition in isolation.

Current analyses further illustrate the impact that secondary gain may have on MMPI-2/RF presentation, even among participants who are not evaluated in an explicitly forensic context. Contrary to expectation, psychological presentations among participants evaluated in a clinical setting were quite comparable with those evaluated in a forensic setting, and it was reasoned that secondary gain issues may have in part accounted for this. Retrospective analyses confirmed that more than one-half of the clinical participants had pending service-connection disability claims for concussion,

psychological difficulties, pain, and/or other health issues, compared with only 20.9% of the research participants. Only 28 of the OEF/OIF clinical participants were technically eligible to submit a disability claim (15 were active military and therefore not yet eligible). Of these, 24 (85.7%) were seeking a disability claim.

In other words, most of the current clinical participants had incentive to exaggerate self-report of emotional and physical symptoms, and the lack of significant differences between the forensic and clinical groups on MMPI-2/RF presentation may reflect the pervasive nature of secondary gain in VA settings. As veterans frequently initiate compensation and pension claims coincident with their clinical care, it may be artificial to assume that researchers are able to discretely segregate individuals with and without incentive to exaggerate. Speaking specifically to the issue of feigned cognitive symptoms in OEF/OIF samples, Armistead-Jehle (2010, p. 58) suggested that, “dividing this population into groups that have and do not have a clear external incentive to appear cognitively compromised may be an impossible task”.

Alternatively, for a portion of the clinical sample, significant elevations on validity and clinical scales may have reflected a manifestation of psychological distress independent of, or conjoined with, secondary gain issues. It has been our clinical experience that the pattern of presentation for many OEF/OIF personnel with persisting PCS seems suggestive of a somatoform disorder consisting of non-credible symptoms that are compellingly disproportionate to the mild nature and severity of the concussive injury. Physiatrists and other Polytrauma providers often refer OEF/OIF personnel for neuropsychological evaluation on the very basis of the complexity of their symptom presentation and, oftentimes, patients’ limited response to rehabilitative therapeutic efforts. In the current Polytrauma setting, OEF/OIF veterans are often administered the MMPI-2/RF only if there is preconceived concern regarding the nature and extent of emotional difficulties, chronic pain, alcohol or other substance dependency difficulties. Thus, this may represent a sampling bias in the current clinical

group and exemplify what has been referred to as “the most problematic differential diagnosis”; that is, making the determination between somatoform disorder and malingering (Boone, 2007, p. 30).

Therefore, for some OEF/OIF personnel, moderate elevations on select MMPI-2/RF validity scales may reflect an subconscious magnification of genuine symptoms as opposed to intentional exaggeration of symptoms to obtain an external incentive (malingering). Particularly for a veteran population, the potential for an interaction effect, or co-occurrence, of strong external incentives (disability income) with somatoform symptoms is also plausible and merits further investigation. Kay et al. (1992, p. 380), for example, argue that individuals in litigation are much less likely to consciously malinger than to assume a “motivated but unconscious” tendency of “holding onto symptoms,” especially if “financial hopes are being pinned on the outcome of the suit”. Accordingly, it is possible that the similarities between the clinical and forensic samples reflect symptom exaggeration owing to both secondary gain and somatoform presentation. Consistent with the recommendation of others (Elhai et al., 2000), the MMPI-2 should be used only as a screening tool, and not be used in isolation as suggesting definitive signs of malingering.

These findings also speak to the importance of presenting not only mean group differences in MMPI-2 concussion research, but also rates of clear symptom exaggeration according to well established cut-scores. To present only the former can be misleading. The majority of OEF/OIF veterans who completed the MMPI-2 in the current study did not show evidence of response invalidity. For example, across the three evaluation settings, only 6.3% of the sample demonstrated an FBS elevation that was at or above T-100, a level of symptom endorsement that has been identified with almost certain exaggeration of somatic symptoms (Greiffenstein et al., 2008). Only 6.3% of the participants elevated at or above T-100 on Fs, and only 2.3% of the current participants elevated at T-119 on RBS, levels of symptom endorsement that would suggest clear over-report of symptoms. It is noteworthy that all eight of the participants who demonstrated FBS T-scores above 100 had: (a) a

previous PTSD diagnosis, and (b) active disability claims. Although current results did not reveal a significant interaction effect between Axis I diagnosis and disability claim status, the latter finding raises the possibility that such an effect could be present in larger concussion samples.

Unexpectedly, Fs did not demonstrate group differences in the current study. Unlike Wygant et al. (2009), who found a large effect size difference for Fs between head injury simulators and head injured controls (Cohen's *d* = .90), Fs was not meaningfully different across evaluation contexts, or as a function of compensation-seeking status in this study. It is plausible that this reflects methodological differences between Wygant et al. and the current study. For instance, Wygant and colleagues included a group of head injury simulators who were instructed to exaggerate their symptoms, whereas the current participants underwent 'real world' neuropsychological evaluation related to a history of concussion. Additionally, the majority of the current sample presented with varied psychiatric co-morbidities, including PTSD, which may have attenuated some of the unique, infrequent somatic complaints that Fs was designed to detect. Further research is needed to further inform Fs interpretative guidelines in concussion samples evaluated in diverse clinical settings (both military and civilian).

Current results have clear implications for the treatment of OEF/OIF veterans with reported histories of concussion and other co-morbidities. For many clinicians, the MMPI-2 plays a vital role in the comprehensive assessment of psychological/adaptive difficulties that may bear relevance to rehabilitation (Arbisi & Ben-Porath, 1999). Current findings illustrate that OEF/OIF veterans with histories of concussion are most likely to elevate on RCd, RC1, RC2, and RF Special Problem scales. Psychotherapies aimed at alleviating depression, post-traumatic stress, chronic pain, and other post-deployment stressors are essential to the recovery process in the late stage of combat-related concussion. Therapeutic assessment (see Finn, 1996) could assist the clinician and patient in understanding PCS and their strong overlap with emotional disorders. Following the intervention models proposed by others (Mittenberg et al., 1996; Ponsford et al., 2001), psychoeducation regarding

the natural trajectory of recovery following concussion should be considered in the therapy process in the hope of promoting favorable long-term recovery.

It is interesting to note the relative normality of MMPI-2/RF scales among the 12 participants who did not have active disability claims or Axis I conditions in the current study (see Table 6). Profiles of this subgroup appear to be consistent with those of a concussion sample presented by Arbisi et al., in press). In the latter study, a subgroup of 33 veterans who had screened positive for concussion (but not PTSD) demonstrated comparable MMPI-2/RF profiles relative to a control group (with neither PTSD nor concussion), and both groups as a whole did not show signifcaint elevations on validity, RC, or SP scales. While additional research with more sizeable OEF/OIF concussion samples is needed, this result would suggest that remote concussion in and of itself does not typically contribute to significant physical or psychological symptoms independent of PTSD and other forms of psychological distress in the late stage of injury, a finding that has been reported by survey researchers (Hoge et al., 2008; Polusny et al., 2011; Schneidermann et al., 2008).

Limitations of the current study should be emphasized. First, all of the current MMPI-2/RF profiles were obtained in the context of a *neuropsychological evaluation* related to a history of *concussion*. It should not be assumed that current findings are applicable outside of an explicitly neuropsychological context or when concussion is not the condition being evaluated. In fact, MMPI-2/RF presentations are likely to vary substantially outside of the neuropsychology context. For example, although Fp was rarely elevated in the current concussion sample, a substantial literature base demonstrates that Fp is among the most effective scale to detect feigned psychopathology, such as PTSD symptoms, in civilian trauma samples (Bury & Bagby, 2002; Elhai et al., 2001; Elhai et al., 2004). Similarly, while somatic (e.g., RC1, MLS) and cognitive (e.g., COG) symptoms were the most prevalent in the current concussion sample, other significant symptom patterns are likely to be observed in non-concussion samples, such as non-concussion PTSD samples, wherein heightened

symptoms of anxiety may be disproportionate (e.g., RC6, AXY) relative to somatic and cognitive complaints. Similar to Arbisi et al. (in press), future researchers might compare MMPI-2/RF profiles of OEF/OIF PTSD concussion samples with OEF/OIF samples with PTSD in isolation to better understand disparate presentation patterns.

Second, this preliminary study of MMPI-2/RF presentation in OEF/OIF concussion samples implemented a differential prevalence design, a methodology that has been widely criticized (Rogers, 2008). Unlike known-groups designs, which identify groups of interest on the basis of an independent criterion, the current study rested upon the assumption that presentation would vary by certain contextual factors (e.g., forensic evaluation context; presence of active disability claim). The reader should be mindful of this limitation when interpreting present findings. For example, identification of possible symptom exaggeration in the current study was based upon previously recommended cut-scores. Until results of a more rigorous methodology (e.g., known-groups) are reported in OEF/OIF concussion samples, with or without co-morbid PTSD, definitive cut-scores of 'probable' and 'definite' symptom exaggeration on MMPI-2/RF validity scales will remain unclear. Future researchers are encouraged to examine differential patterns of MMPI-2/RF presentation in OEF/OIF concussion samples when group assignment can be more clearly delineated by an independent gold standard. For example, future researchers might identify groups according to effort performances and observe MMPI-2/RF validity scale differences in those with sufficient versus insufficient effort. Researchers might also explore the incremental validity of effort measures and psychological response validity instruments in OEF/OIF cohorts, as has been conducted in previous civilian samples (e.g., Nelson et al., 2007; Smart et al., 2008; Wygant et al., in press).

Finally, the current study examined MMPI-2/RF profiles in OEF/OIF participants with histories of mild traumatic brain injury (concussion), most of whom had histories of PTSD or other Axis I co-morbidity. For the most part, the sample cannot be considered to be a 'pure' concussion sample, and

this limits an understanding of MMPI-2/RF presentation on the basis of concussion alone. Indeed, identifying individuals with histories of combat-related concussion and without psychological co-morbidities is exceedingly difficult, which is reflected in the relatively few individuals who reported this history in the current study.

In summary, current findings suggest that rates of possible symptom exaggeration, particularly over-endorsement of somatic and cognitive symptoms, increases dramatically in forensic and clinical contexts relative to settings in which primary and secondary gain issues are less salient to OEF/OIF concussion groups. Clinical neuropsychologists are encouraged to be mindful of the impact that secondary gain may have on MMPI-2/RF presentation regardless of the context in which the instrument was administered (forensic, clinical, or research).

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Table 1. Demographics by evaluation context.

	Evaluation Context			
	Forensic (n = 42)	Clinical (n = 43)	Research (n = 43)	
Variable	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*
Age (years)	30.5 (8.9)	31.7 (8.8)	33.1 (8.1)	1.0
Education (years)	12.6 (1.8)	12.9 (1.6)	14.3 (1.9)	11.3***
Concussions (number)	1.6 (0.9)	3.0 (3.4)	6.0 (6.2)	12.5***
Time since most recent concussion (months)	32.3 (21.0)	33.7 (16.1)	41.2 (17.2)	2.9
	n (%)	*n* (%)	*n* (%)	χ^2
Injury parameter				17.4**
LOC	6 (16.7)	21 (48.8)	17 (39.5)	
AMS	25 (59.5)	14 (32.6)	10 (23.8)	
No LOC (Neurologic signs only)	10 (23.8)	8 (18.6)	16 (37.2)	
Axis I Diagnosis				6.5
PTSD+	20 (47.6)	21 (48.8)	17 (39.5)	
Other (no PTSD)	16 (38.1)	16 (37.2)	13 (30.2)	
None	6 (14.3)	6 (9.3)	13 (30.2)	

Note. **p =.002; ***p < .001. 'PTSD+' indicates history of formal diagnosis of PTSD alone, or PTSD with co-morbid psychological condition (e.g., depression, substance dependence). 'Other' indicates negative history of PTSD, but positive history of other Axis I diagnosis (e.g., depression, anxiety, substance dependence).

Table 2. MMPI-2 and MMPI-2-RF scales by evaluation context.

	Evaluation Context						
	Forensic (n = 42)	Clinical (n = 43)	Research (n = 43)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
F	68.5 (14.4)	67.5 (18.1)	59.0 (15.1)	4.60	.65	.51	.08
F-r	74.2 (19.4)[a]	77.5 (22.7)[a]	62.7 (20.9)	5.84**	.57	.68	-.13
Fb	62.5 (16.7)	64.4 (20.6)	55.1 (15.6)	3.28	.46	.51	-.09
Fp	53.8 (13.4)	56.2 (13.9)	51.1 (7.7)	2.02	.25	.46	-.18
Fp-r	60.2 (13.7)	61.2 (15.6)	53.6 (10.2)	4.12	.55	.58	-.07
FBS	78.0 (15.7)[a]	77.4 (16.9)[a]	61.1 (12.0)	17.51***	1.21	1.11	.05
FBS-r	74.3 (14.0)[a]	73.5 (15.2)[a]	58.9 (12.1)	16.80***	1.18	1.06	.07
RBS	82.2 (15.8)[a]	80.3 (19.2)[a]	67.7 (19.1)	8.15***	.83	.64	.13
Fs	75.4 (19.5)	70.2 (21.2)	66.0 (13.8)	2.75	.56	.24	.28
RC Scales							
RCd	62.3 (11.6)[a]	62.9 (12.1)[a]	54.0 (12.2)	7.48***	.70	.74	-.03
RC1	73.8 (12.8)[a]	71.2 (14.4)[a]	60.5 (12.8)	11.95***	1.04	.79	.22
RC2	62.4 (14.9)[a]	65.6 (15.0)[a]	51.8 (13.7)	10.67***	.74	.96	-.20
RC3	52.3 (9.9)	54.8 (13.2)	56.4 (12.9)	1.27	-.36	-.13	-.20
RC4	55.8 (10.9)	52.9 (11.5)	52.2 (8.1)	1.51	.38	.00	.27
RC6	54.1 (11.1)	57.9 (15.2)	52.3 (11.9)	2.06	.15	.40	-.26

(*Table continues*)

	Evaluation Context						
	Forensic (n = 42)	Clinical (n = 43)	Research (n = 43)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
RC7	58.6 (12.8)	60.0 (12.6)	54.5 (13.0)	2.16	.32	.43	-.09
RC8	57.0 (10.4)	56.1 (12.5)	55.6 (12.1)	.15	.12	.04	.09
RC9	53.2 (10.7)	55.9 (11.2)	54.6 (10.0)	.65	-.13	.12	-.23
RF SP Scales							
MLS	69.3 (14.4)[a]	72.9 (12.4)[a]	59.5 (13.7)	11.2***	.70	1.03	-.27
GIC	63.2 (16.8)[a]	61.9 (17.5)	53.3 (11.5)	5.1*	.68	.57	.08
HPC	69.2 (12.2)[a]	67.6 (14.1)[a]	57.3 (10.9)	11.4***	1.03	.82	.12
NUC	72.1 (12.9)[a]	71.9 (14.9)[a]	60.6 (13.4)	9.7***	.87	.80	.01
COG	75.6 (12.3)[a]	75.3 (13.2)[a]	65.5 (16.9)	6.9***	.68	.65	.02
SUI	49.1 (9.6)	52.2 (14.7)	49.9 (11.8)	0.74	-.07	.17	-.25
HLP	53.9 (14.1)	56.4 (13.6)	50.0 (10.5)	2.68	.31	.53	-.18
SFD	54.9 (12.9)	57.5 (12.4)	50.7 (9.5)	3.81	.37	.62	-.21
NFC	56.1 (10.4)	55.5 (12.1)	51.7 (10.8)	2.02	.41	.33	.05
STW	55.2 (13.1)[a]	59.1 (11.9)[a]	50.0 (11.1)	6.08*	.43	.79	-.31
AXY	71.5 (16.2)	68.6 (13.1)	63.2 (18.3)	2.94	.48	.34	.20
ANP	62.9 (13.2)	64.4 (11.8)	57.7 (12.7)	3.36	.40	.55	-.12
BRF	52.2 (9.3)	51.9 (11.8)	47.7 (8.9)	2.67	.50	.40	.03
MSF	43.5 (6.6)	44.1 (6.9)	44.2 (5.6)	0.12	-.11	-.01	-.09

Note. *$p < .01$, **$p < .005$; ***$p < .001$. [a]Significantly different from Research group. '*d*1', '*d*2', and '*d*3' denote effect size differences between the forensic/research groups, the clinical/research groups, and forensic/clinical groups, respectively. RC = MMPI-2 Restructured Clinical Scales; SP = MMPI-2-Restructured Form Special Problem Scales; MLS = Malaise; GIC = Gastrointestinal Complaints; HPC = Head Pain Complaints; NUC = Neurological Complaints; COG = Cognitive Complaints; SUI = Suicidal/Death Ideation; HLP = Helplessness/Hopelessness; SFD = Self-Doubt; NFC = Inefficacy; STW = Stress/Worry; AXY = Anxiety; ANP = Anger Proneness; BRF = Behavior-Restricting Fears; MSF = Multiple Specific Fears.

Table 3. Frequencies of MMPI-2 and MMPI-2-RF validity scale elevations by evaluation context.

	Evaluation Context			
	Forensic[a]	Clinical[b]	Research[c]	Full Sample[d]
Validity Scale	*n* (%)	*n* (%)	*n* (%)	*n* (%)
F (*T*)				
>69	21 (50.0)	14 (32.6)	9 (20.9)	44 (34.4)
>79	9 (21.4)	7 (16.3)	3 (7.0)	19 (14.8)
>89	3 (7.1)	6 (14.0)	2 (4.7)	11 (8.6)
>99	1 (2.4)	5 (11.6)	1 (2.3)	7 (5.5)
>119	0 (0.0)	1 (2.3)	0 (0.0)	1 (0.8)
F-r (*T*)				
>69	25 (59.5)	26 (60.5)	14 (32.6)	65 (50.8)
>79	18 (42.9)	14 (32.6)	7 (16.3)	39 (30.5)
>89	8 (19.0)	10 (23.3)	4 (9.3)	22 (17.2)
>99	5 (11.9)	10 (23.3)	4 (9.3)	19 (14.8)
>119	1 (2.4)	4 (9.3)	1 (2.3)	6 (4.7)
Fb (*T*)				
>69	15 (35.7)	12 (27.9)	7 (16.3)	34 (26.6)
>79	5 (11.9)	8 (18.6)	3 (7.0)	16 (12.5)
>89	2 (4.8)	6 (14.0)	2 (4.7)	10 (7.8)
>99	1 (2.4)	4 (9.3)	1 (2.3)	6 (4.7)
>119	0 (0.0)	2 (4.7)	0 (0.0)	2 (1.6)
Fp (*T*)				
>69	7 (16.7)	9 (20.9)	1 (2.3)	17 (13.3)
>79	2 (4.8)	2 (4.7)	0 (0.0)	4 (3.1)
>89	1 (2.4)	1 (2.3)	0 (0.0)	2 (1.6)
>99	0 (0.0)	1 (2.3)	0 (0.0)	1 (0.8)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fp-r (*T*)				
>69	5 (11.9)	7 (16.3)	1 (2.3)	13 (10.2)
>79	3 (7.1)	2 (4.7)	1 (2.3)	6 (4.7)
>89	1 (2.4)	2 (4.7)	1 (2.3)	4 (3.1)
>99	1 (2.4)	2 (4.7)	0 (0.0)	3 (2.3)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

(*Table continues*)

	Evaluation Context			
	Forensic[a]	Clinical[b]	Research[c]	Full Sample[d]
Validity Scale	*n* (%)	*n* (%)	*n* (%)	*n* (%)
FBS (*T*)				
>69	28 (66.7)	29 (67.4)	10 (23.3)	67 (52.3)
>79	22 (52.4)	23 (53.5)	2 (4.7)	47 (36.7)
>89	10 (23.8)	9 (20.9)	1 (2.3)	20 (15.6)
>99	3 (7.1)	5 (11.6)	0 (0.0)	8 (6.3)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FBS-r (*T*)				
>69	25 (59.5)	27 (62.8)	10 (23.3)	62 (48.4)
>79	16 (38.1)	20 (46.5)	2 (4.7)	38 (29.7)
>89	9 (21.4)	6 (14.0)	1 (2.3)	16 (12.5)
>99	1 (2.4)	0 (0.0)	0 (0.0)	1 (0.8)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RBS (*T*)				
>69	33 (78.6)	32 (74.4)	20 (46.5)	85 (66.4)
>79	28 (66.7)	24 (55.8)	12 (27.9)	64 (50.0)
>89	13 (31.0)	11 (25.6)	5 (11.6)	29 (22.7)
>99	5 (11.9)	7 (16.3)	3 (7.0)	15 (11.7)
>119	0 (0.0)	2 (4.7)	0 (0.0)	2 (1.6)
Fs (*T*)				
>69	24 (57.1)	18 (41.9)	14 (32.6)	56 (43.8)
>79	18 (42.9)	12 (27.9)	9 (20.9)	39 (30.5)
>89	12 (28.6)	8 (18.6)	5 (11.6)	25 (19.5)
>99	3 (7.1)	5 (11.6)	0 (0.0)	8 (6.3)
>119	0 (0.0)	2 (4.7)	0 (0.0)	2 (1.6)

Note. [a]$n = 42$; [b]$n = 43$; [c]$n = 43$; [d]$N = 128$.

Table 4. MMPI-2 and MMPI-2-RF validity scales by disability claim status.

	Disability Claim Status			
	Active Claim (n = 66)	No Active Claim (n = 53)		
Scale	*M* (*SD*)	*M* (*SD*)	*F*	*d*
Validity Scales				
F	68.7 (16.1)	61.2 (14.8)	4.34	.48
F-r	76.6 (21.4)	66.3 (20.7)	3.19	.49
Fb	63.7 (18.1)	58.3 (18.4)	0.73	.30
Fp	54.3 (14.1)	54.1 (9.0)	0.11	.02
Fp-r	60.7 (14.5)	56.1 (11.8)	2.31	.34
FBS	78.3 (16.2)	65.9 (15.9)	10.22	.77
FBS-r	74.8 (14.3)	63.2 (15.0)	11.80*	.79
RBS	82.4 (17.8)	71.3 (18.3)	6.63	.62
Fs	74.2 (20.6)	66.5 (15.8)	4.52	.41
RC Scales				
RCd	63.1 (11.6)	56.9 (13.0)	3.78	.51
RC1	73.3 (14.2)	63.5 (13.2)	9.79	.71
RC2	63.2 (14.7)	57.2 (16.0)	1.31	.39
RC3	52.8 (11.1)	57.0 (12.9)	2.07	-.35
RC4	55.2 (11.2)	51.5 (9.1)	2.82	.36
RC6	55.4 (13.7)	54.6 (12.2)	0.01	.06

(*Table continues*)

	Disability Claim Status			
	Active Claim (n = 66)	No Active Claim (n = 53)		
Scale	*M* (*SD*)	*M* (*SD*)	*F*	*d*
RC Scale				
RC7	59.7 (12.7)	56.6 (12.7)	0.94	.24
RC8	57.9 (11.6)	53.9 (10.4)	2.42	.36
RC9	54.6 (11.1)	55.0 (10.3)	0.21	-.03
RF SP Scales				
MLS	71.0 (13.4)	63.3 (14.6)	9.80*	.55
GIC	63.6 (17.1)	55.1 (14.0)	4.91*	.54
HPC	69.1 (13.8)	60.3 (11.6)	6.83*	.68
NUC	72.4 (14.6)	63.8 (13.4)	3.90	.61
COG	76.4 (12.5)	68.2 (15.4)	7.43*	.59
SUI	51.0 (13.3)	50.2 (11.5)	1.74	.06
HLP	55.4 (14.6)	51.6 (10.9)	2.36	.29
SFD	55.9 (12.6)	53.4 (11.6)	3.70	.21
NFC	56.3 (11.1)	53.3 (11.6)	1.59	.27
STW	57.5 (13.2)	52.1 (10.8)	6.37*	.44
AXY	71.2 (15.3)	64.5 (16.9)	5.93*	.42
ANP	64.4 (12.4)	59.6 (12.6)	5.91*	.38
BRF	52.3 (10.2)	49.3 (10.5)	1.66	.29
MSF	42.9 (6.0)	45.3 (6.8)	-1.27	-.38

Note. *$p \leq .001$. Three separate analyses were conducted for validity scales, RC scales, and SP scales. The 'active duty' sample does not include 9 research participants who indicated pending disability claims. RC = MMPI-2 Restructured Clinical Scales; SP = MMPI-2-Restructured Form Special Problem Scales; MLS = Malaise; GIC = Gastrointestinal Complaints; HPC = Head Pain Complaints; NUC = Neurological Complaints; COG = Cognitive Complaints; SUI = Suicidal/Death Ideation; HLP = Helplessness/Hopelessness; SFD = Self-Doubt; NFC = Inefficacy; STW = Stress/Worry; AXY = Anxiety; ANP = Anger Proneness; BRF = Behavior-Restricting Fears; MSF = Multiple Specific Fears.

Table 5. MMPI-2 Validity, RC, and RF SP scales by co-morbid Axis I diagnosis.

	Co-Morbid Axis I Diagnosis						
	PTSD+ (n = 59)	Other (n = 45)	None (n = 24)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
Validity							
F	70.7 (16.3)[a]	63.6 (14.4)	53.4 (14.0)	7.65*	1.10	0.72	0.46
F-r	79.6 (21.3)[a]	69.9 (19.0)	54.3 (18.0)	9.75*	1.24	0.84	0.48
Fb	67.5 (19.2)[a]	58.6 (16.1)	47.6 (8.4)	9.51*	1.18	0.79	0.50
Fp	56.4 (12.6)	51.3 (12.0)	51.5 (9.7)	2.62	0.41	-0.02	0.41
Fp-r	62.3 (13.5)	57.1 (14.0)	50.8 (9.9)	4.71	0.91	0.49	0.38
FBS	77.7 (16.9)[a]	71.4 (14.1)	59.7 (14.7)	8.45*	1.10	0.82	0.40
FBS-r	74.2 (14.8)[a]	68.6 (12.7)	56.5 (15.2)	8.25*	1.19	0.89	0.40
RBS	83.5 (15.8)[a]	76.3 (18.1)	60.8 (19.4)	9.04*	1.34	0.84	0.43

(*Table continues*)

	Co-Morbid Axis I Diagnosis						
	PTSD+ (n = 59)	Other (n = 45)	None (n = 24)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
Fs	75.9 (19.3)	67.1 (14.7)	63.7 (20.6)	3.96	0.62	0.20	0.50
RC Scales							
RCd	64.9 (10.8)[a]	59.1 (11.8)	48.1 (10.2)	12.89*	1.58	0.98	0.52
RC1	73.4 (14.1)	67.2 (12.5)	58.6 (13.6)	6.31	1.06	0.67	0.46
RC2	64.6 (15.0)[a]	60.9 (15.1)[a]	46.5 (9.8)	9.49*	1.32	1.07	0.25
RC3	55.6 (12.2)	55.1 (12.6)	50.8 (10.7)	1.13	0.41	0.36	0.04
RC4	57.0 (10.1)[a]	52.1 (10.6)	48.1 (7.1)	7.08*	0.95	0.42	0.47
RC6	57.1 (14.6)	53.3 (12.1)	51.8 (9.1)	1.26	0.40	0.13	0.28
RC7	62.0 (12.3)[a]	57.5 (11.2)	47.4 (11.7)	7.67*	1.20	0.89	0.38
RC8	59.7 (11.0)	54.0 (11.8)	51.9 (11.0)	6.71	0.71	0.18	0.50

(*Table continues*)

	Co-Morbid Axis I Diagnosis						
	PTSD+ (n = 59)	Other (n = 45)	None (n = 24)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
RC9	56.7 (11.4)	52.9 (9.0)	52.4 (10.9)	2.08	0.38	0.05	0.36
RF SP Scales							
MLS	72.2 (12.4)[a]	69.0 (13.2)[a]	51.8 (11.7)	15.32*	1.67	1.35	0.25
GIC	65.6 (16.7)[a]	55.6 (14.2)	51.4 (11.5)	7.66*	0.92	0.31	0.64
HPC	68.9 (13.2)	64.2 (12.0)	55.3 (12.3)	4.68	1.05	0.74	0.37
NUC	71.5 (15.8)	68.0 (12.5)	60.2 (13.1)	2.29	0.75	0.61	0.24
COG	77.3 (13.0)[a]	72.3 (11.3)[a]	58.8 (17.3)	11.12*	1.29	0.99	0.41
SUI	53.3 (15.0)	48.7 (9.8)	46.8 (5.9)	2.69	0.50	0.22	0.35
HLP	56.2 (14.8)	52.6 (11.8)	48.0 (7.8)	3.15	0.62	0.43	0.26
SFD	58.9 (11.9)[a]	52.3 (11.5)	47.0 (7.4)	8.11*	1.10	0.52	0.56

(*Table continues*)

	Co-Morbid Axis I Diagnosis						
	PTSD+ (n = 59)	Other (n = 45)	None (n = 24)				
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*F*	*d*1	*d*2	*d*3
NFC	56.6 (9.7)	54.8 (13.4)	48.3 (7.9)	2.69	0.90	0.55	0.16
STW	58.9 (12.0)[a]	54.9 (12.3)	44.4 (7.2)	11.12*	1.34	0.97	0.33
AXY	73.8 (14.3)[a]	67.3 (15.2)	53.7 (14.2)	10.26*	1.41	0.91	0.44
ANP	67.1 (10.9)[a]	60.3 (12.1)	50.9 (11.0)	11.82*	1.48	0.80	0.59
BRF	53.1 (11.5)	49.6 (9.4)	46.5 (6.4)	2.58	0.64	0.37	0.33
MSF	44.5 (6.5)	43.7 (6.0)	43.0 (6.8)	1.01	0.23	0.11	0.13

Note. *$p \leq .001$. [a]Denotes significantly higher elevations relative to the 'None' group. Axis I diagnoses are in addition to, and independent from, self-reported concussion. PTSD+ = formal PTSD diagnosis alone or in conjunction with additional Axis I condition; 'Other I' = condition other than PTSD (e.g., depression, anxiety, substance dependence). '*d*1', '*d*2', and '*d*3' denote effect size differences between the PTSD+/None groups, the Other/None groups, and the PTSD+/Other groups, respectively. RC = MMPI-2 Restructured Clinical Scales; SP = MMPI-2-Restructured Form Special Problem Scales; MLS = Malaise; GIC = Gastrointestinal Complaints; HPC = Head Pain Complaints; NUC = Neurological Complaints; COG = Cognitive Complaints; SUI = Suicidal/Death Ideation; HLP = Helplessness/Hopelessness; SFD = Self-Doubt; NFC = Inefficacy; STW = Stress/Worry; AXY = Anxiety; ANP = Anger Proneness; BRF = Behavior-Restricting Fears; MSF = Multiple Specific Fears.

Table 6. MMPI-2 validity, RC, RF SP scales by claim and co-morbid diagnosis.

	Active Claim (*n* = 66)			No Active Claim (*n* = 53)		
	PTSD+ (*n* = 35)	Other (*n* = 24)	None (*n* = 7)	PTSD+ (*n* = 23)	Other (*n* = 18)	None (*n* = 12)
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Validity						
F	74.1 (15.9)	63.1 (12.4)	60.7 (20.5)	66.3 (15.9)	61.5 (12.9)	51.0 (10.0)
F-r	84.9 (20.7)	69.2 (16.7)	60.4 (23.0)	72.8 (20.1)	67.4 (19.7)	52.4 (17.7)
Fb	69.8 (18.7)	58.9 (15.1)	49.7 (12.1)	65.1 (19.8)	57.6 (18.2)	46.6 (7.3)
Fp	56.2 (13.9)	51.0 (14.7)	56.0 (13.2)	57.5 (10.3)	51.3 (7.1)	52.0 (7.5)
Fp-r	63.5 (14.0)	58.0 (15.1)	55.7 (13.1)	60.9 (12.8)	54.6 (10.3)	49.3 (8.1)
FBS	85.1 (15.3)	72.2 (12.9)	65.4 (16.1)	67.4 (13.2)	71.7 (16.5)	54.3 (14.5)
FBS-r	80.3 (13.4)	70.0 (11.2)	64.0 (17.4)	65.5 (12.0)	67.7 (15.2)	51.9 (15.3)
RBS	88.3 (14.8)	77.8 (17.1)	69.0 (24.0)	77.0 (14.7)	73.0 (19.1)	57.8 (17.8)
Fs	79.5 (21.2)	66.5 (15.9)	73.9 (26.5)	71.4 (14.9)	64.8 (12.3)	59.5 (19.9)
RC Scales						
RCd	67.2 (10.0)	60.3 (11.0)	52.1 (11.8)	62.0 (11.2)	57.2 (13.5)	46.8 (9.9)
RC1	78.7 (12.6)	67.5 (13.2)	66.1 (15.9)	66.1 (13.0)	65.6 (11.9)	55.2 (13.1)
RC2	68.8 (13.4)	59.0 (14.3)	49.3 (7.9)	58.9 (15.4)	59.0 (14.3)	45.3 (10.3)
RC3	51.3 (9.2)	55.4 (13.3)	51.3 (11.4)	62.1 (13.7)	52.5 (11.2)	53.9 (10.8)
RC4	57.7 (11.6)	52.8 (10.8)	51.1 (7.8)	56.3 (7.6)	49.6 (9.8)	45.3 (5.9)
RC6	57.7 (15.7)	52.5 (10.9)	53.1 (10.6)	56.3 (13.5)	53.9 (12.6)	52.6 (9.3)

	Active Claim (n = 66)			No Active Claim (n = 53)		
	PTSD+ (n = 35)	Other (n = 24)	None (n = 7)	PTSD+ (n = 23)	Other (n = 18)	None (n = 12)
Scale	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
RC Scales						
RC7	62.0 (12.9)	58.5 (11.0)	52.0 (14.9)	62.4 (11.8)	55.3 (11.7)	47.4 (10.2)
RC8	60.9 (12.5)	54.5 (9.3)	54.4 (11.5)	58.5 (8.2)	50.0 (10.9)	51.0 (10.6)
RC9	55.3 (12.4)	52.7 (8.9)	57.9 (11.6)	58.7 (9.9)	52.3 (9.7)	51.8 (10.5)
RF SP Scales						
MLS	75.6 (12.1)	68.2 (12.7)	57.9 (11.4)	67.3 (11.4)	68.4 (14.3)	47.9 (10.0)
GIC	69.4 (17.0)	57.5 (15.9)	54.9 (11.4)	60.7 (14.8)	51.8 (12.1)	49.5 (12.1)
HPC	73.9 (12.5)	63.6 (13.4)	63.9 (14.5)	61.7 (10.7)	64.4 (11.1)	51.5 (9.8)
NUC	76.5 (14.3)	68.1 (13.4)	66.6 (15.3)	64.5 (15.4)	66.7 (10.5)	58.0 (12.4)
COG	79.3 (12.3)	75.0 (9.7)	66.7 (17.4)	75.3 (13.4)	68.0 (12.4)	55.0 (15.4)
SUI	54.9 (16.3)	47.3 (8.0)	45.0 (0.0)	51.2 (13.0)	51.1 (12.2)	46.8 (6.1)
HLP	59.4 (15.9)	52.1 (12.6)	46.9 (6.4)	52.1 (12.0)	54.2 (11.0)	46.7 (7.3)
SFD	60.1 (12.0)	52.1 (12.3)	48.1 (8.8)	57.9 (11.6)	52.1 (11.7)	46.8 (7.7)
NFC	57.5 (10.5)	56.0 (12.4)	51.3 (8.9)	55.5 (8.7)	54.4 (15.6)	47.3 (7.6)
STW	62.1 (12.2)	45.4 (7.3)	45.4 (7.3)	55.2 (10.0)	54.3 (11.4)	42.8 (5.6)
AXY	76.5 (13.1)	66.9 (14.0)	59.6 (20.4)	70.4 (15.6)	66.2 (17.6)	50.8 (10.6)
ANP	67.8 (11.3)	62.0 (11.8)	55.3 (15.3)	66.5 (10.7)	57.3 (12.1)	50.1 (9.1)
BRF	54.7 (10.6)	50.3 (9.6)	47.7 (8.3)	51.1 (12.8)	49.0 (9.7)	46.3 (5.9)
MSF	43.6 (6.7)	42.6 (5.0)	40.3 (5.4)	45.7 (6.2)	45.7 (7.1)	44.1 (8.0)

Note. ‘PTSD+’ = formal PTSD diagnosis alone or in conjunction with other Axis I condition; ‘Other’ = Axis I condition other than PTSD (e.g., depression, anxiety, substance dependence). ‘*d*1’, ‘*d*2’, and ‘*d*3’ denote effect size differences between the PTSD+/No diagnosis groups, the Other Axis I (non-PTSD)/No diagnosis groups, and PTSD+/Other Axis I (non-PTSD) groups, respectively. RC = MMPI-2 Restructured Clinical Scales; SP = MMPI-2-Restructured Form Special Problem Scales; MLS = Malaise; GIC = Gastrointestinal Complaints; HPC = Head Pain Complaints; NUC = Neurological Complaints; COG = Cognitive Complaints.

Table 7. MMPI-2/RF validity scale frequencies.

	Active Claim (*n* = 66)			No Active Claim (*n* = 53)		
	PTSD+ (*n* = 35)	Other (*n* = 24)	None (*n* = 7)	PTSD+ (*n* = 23)	Other (*n* = 18)	None (*n* = 12)
Scale	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
F (*T*)						
>69	21 (60.0)	8 (33.3)	1 (14.3)	8 (34.8)	3 (16.7)	1 (8.3)
>79	10 (28.6)	2 (8.3)	1 (14.3)	3 (13.0)	2 (11.1)	0 (0.0)
>89	5 (14.3)	1 (4.2)	1 (14.3)	2 (8.7)	1 (5.6)	0 (0.0)
>99	3 (8.6)	0 (0.0)	1 (14.3)	2 (8.7)	0 (0.0)	0 (0.0)
>119	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
F-r (*T*)						
>69	27 (77.1)	13 (54.2)	1 (14.3)	13 (56.5)	6 (33.3)	2 (16.7)
>79	19 (54.3)	4 (16.7)	1 (14.3)	7 (30.4)	2 (11.1)	1 (8.3)
>89	11 (31.4)	2 (8.3)	1 (14.3)	4 (17.4)	2 (11.1)	1 (8.3)
>99	9 (25.7)	1 (4.2)	1 (14.3)	4 (17.4)	2 (11.1)	1 (8.3)
>119	4 (11.4)	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fb (*T*)						
>69	16 (45.7)	6 (25.0)	1 (14.3)	7 (30.4)	3 (16.7)	0 (0.0)
>79	8 (22.9)	2 (8.3)	0 (0.0)	3 (13.0)	3 (16.7)	0 (0.0)
>89	5 (14.3)	1 (4.2)	0 (0.0)	2 (8.7)	2 (11.1)	0 (0.0)
>99	2 (5.7)	1 (4.2)	0 (0.0)	2 (8.7)	1 (5.6)	0 (0.0)
>119	1 (2.9)	0 (0.0)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
Fp (*T*)						
>69	7 (20.0)	3 (12.5)	2 (28.6)	4 (17.4)	0 (0.0)	0 (0.0)
>79	1 (2.9)	2 (8.3)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
>89	1 (2.9)	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>99	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fp-r (*T*)						
>69	6 (17.1)	2 (8.3)	1 (14.3)	3 (13.0)	0 (0.0)	0 (0.0)
>79	2 (5.7)	2 (8.3)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
>89	1 (2.9)	1 (4.2)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
>99	1 (2.9)	1 (4.2)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Active Claim (n = 66)			No Active Claim (n = 53)		
	PTSD+ (n = 35)	Other (n = 24)	None (n = 7)	PTSD+ (n = 23)	Other (n = 18)	None (n = 12)
Scale	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
FBS (T)						
>69	31 (88.6)	11 (45.8)	2 (28.6)	9 (39.1)	10 (55.6)	2 (16.7)
>79	25 (71.4)	8 (33.3)	2 (28.6)	5 (21.7)	6 (33.3)	1 (8.3)
>89	14 (40.0)	3 (12.5)	0 (0.0)	0 (0.0)	2 (11.1)	0 (0.0)
>99	8 (22.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FBS-r (T)						
>69	28 (80.0)	11 (45.8)	2 (28.6)	9 (39.1)	9 (50.0)	2 (16.7)
>79	19 (54.3)	6 (25.0)	2 (28.6)	4 (17.4)	6 (33.3)	1 (8.3)
>89	11 (31.4)	2 (8.3)	1 (14.3)	1 (4.3)	1 (5.6)	0 (0.0)
>99	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>119	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RBS (T)						
>69	31 (88.6)	17 (70.8)	3 (42.9)	17 (73.9)	11 (61.1)	2 (16.7)
>79	28 (80.0)	13 (54.2)	2 (28.6)	12 (52.2)	6 (33.3)	2 (16.7)
>89	16 (45.7)	4 (16.7)	1 (14.3)	3 (13.0)	3 (16.7)	1 (8.3)
>99	7 (20.0)	2 (8.3)	1 (14.3)	1 (4.3)	2 (11.1)	1 (8.3)
>119	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fs (T)						
>69	23 (65.7)	8 (33.3)	3 (42.9)	12 (52.2)	5 (27.8)	2 (16.7)
>79	20 (57.1)	5 (20.8)	2 (28.6)	5 (21.7)	2 (11.1)	2 (16.7)
>89	13 (37.1)	2 (8.3)	2 (28.6)	3 (13.0)	2 (11.1)	2 (16.7)
>99	4 (11.4)	1 (4.2)	1 (14.3)	1 (4.3)	0 (0.0)	1 (8.3)
>119	1 (2.9)	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)

Note. ‘PTSD+’ = formal PTSD diagnosis alone or in conjunction with other Axis I condition; ‘Other’ = Axis I condition other than PTSD (e.g., depression, anxiety, substance dependence).